Cover Letter

XXX

Form Approved. O.M.B. Nos. 2070-0012 and 2070-0038

U.S. ENVIRONMENTAL PROTECTION AGENCY			AGENCY USE ONLY
EPA	PREMANUFACTURE NOTICE FOR NEW CHEMICAL SUBSTANCES		Date of receipt: 03/13/2020
When completed, send this form to:	If sending by Courier: Office of Pollution Prevention and Toxics Document Control Office (7407M) US EPA, 1201 Constitution Ave NW WASHINGTON, D.C. 20460 Contact Numbers: 202-564-8930/8940	If sending by US Mail: Office of Pollution Prevention and Toxics Document Control Office (7407M) US EPA, 1200 Pennsylvania Ave NW WASHINGTON, D.C. 20460	Submission Report Number

Total Number of Pages	TS Number
20	AB62JB

GENERAL INSTRUCTIONS

- You must provide all information requested in this form to the extent that it is known to or reasonably ascertainable by you. Make reasonable estimates if you do not have actual data.
- Before you complete this form, you should read the "Instructions Manual for Premanufacture Notification" (the Instructions Manual is available from the Toxic Substances Control Act (TSCA) Information Service by calling 202-554-1404, or faxing 202-554-5603).
- If a fee has been remitted for this notice (40 CFR 700.45), indicate in the boxes above the TS fee identification number you have generated. Remember, your fee ID number must also appear on your corresponding fee remittance. For mailing address information see the Help instructions in the e-PMN tool.

Part I – GENERAL INFORMATION

You must provide the currently correct Chemical Abstracts (CA) Name of the new chemical substance, even if you claim the identity as confidential. You may authorize another person to submit chemical identity information for you, but your submission will not be complete and the review will not begin until EPA receives this information. A letter in support of your submission should reference your TS fee identification number. For all Section 5 Notice submissions (paper or electronic) you must submit an original notice including all test data; if you claimed any information as confidential, an original sanitized copy must also be submitted.

Part II – HUMAN EXPOSURE AND ENVIRONMENTAL RELEASE

If there are several manufacture, processing, or use operations to be described in Part II, sections A and B of this notice, reproduce the sections as needed.

Part III – LIST OF ATTACHMENTS

For paper submissions, attach additional sheets if there is not enough space to answer a question fully. Label each continuation sheet with the corresponding section heading. In Part III, list these attachments, any test data or other data and any optional information included in the notice.

OPTIONAL INFORMATION

You may include any information that you want EPA to consider in evaluating the new substance. On page 11 of this form, space has been provided for you to describe pollution prevention and recycling information you may have regarding the new substance. "Binding" boxes are included throughout this form for you to indicate your willingness to be bound to certain statements you make in this section, such as use, production volume, protective equipment . . . The intention is to reduce delays that routinely accompany the development of consent orders or Significant New Use Rules. Checking a "binding" box in a PMN does not by itself prohibit the submitter from later deviating from the information (except chemical identity) reported in the form; however, in the case of exemption applications (such as TMEA, LVE, LOREX) certain information provided in such notifications is binding on the submitter when the Agency approves the exemption application, especially if the production volume "binding" box is chosen in a LVE.

CONFIDENTIALITY CLAIMS

You may claim any information in this notice as confidential. To assert a claim on the form, mark (X) the confidential box next to the information that you claim as confidential. To assert a claim in an attachment, circle or bracket the information you claim as confidential. If you claim information in the notices as confidential, you must also provide a sanitized version of the notice, (including attachments). For additional instructions on claiming information as confidential, read the Instructions Manual.

TEST DATA AND OTHER DATA

You are required to submit all test data in your possession or control and to provide a description of all other data known to or reasonably ascertainable by you, if these data are related to the health and environmental effects on the manufacture, processing, distribution in commerce, use, or disposal of the new chemical substance. Standard literature citations may be submitted for data in the open scientific literature. Complete test data (written in English), not summaries of data, must be submitted if they do not appear in the open literature. You should clearly identify whether test data is on the substance or on an analog. Also, the chemical composition of the tested material should be characterized. Following are examples of test data and other data. Data should be submitted according to the requirements of §720.50 of the Premanufacture Notification Rule (40 CFR Part 720).

Test Data (Check Below any included in this notice)

☐	Environmental fate data	☐	Other Data
X	Health effects data	☐	Risk Assessments
☐	Environmental effects data	☐	Structure/activity relationships
X	Physical/Chemical Properties (A physical and chemical properties worksheet is located on the last page of this form.)		
☐	Test data not in the possession or control of the submitter		

TYPE OF NOTICE (Check Only One)

X	**PMN** (Premanufacture Notice)
☐	**SNUN** (Significant New Use Notice)
☐	**TMEA** (Test Marketing Exemption Application)
☐	**LVE** (Low Volume Exemption) @ 40 CFR 723.50(c)(1)
☐	**LOREX** (Low Release/Low Exposure Exemption) @ 40 CFR 723.50(c)(2)
☐	**LVE** Modification
☐	**LOREX** Modification
☐	**Mock Submission**
☐	Mark (X) if pending Letter of Support
N	IS THIS A CONSOLIDATED PMN (Y/N)?
1	# of chemicals or polymers (Prenotice Communication # required, enter # on p. 3).
X	Mark (X) if any information in this notice is claimed as confidential.

The public reporting and recordkeeping burden for this collection of information is estimated to average 93 hours per response. Send comments on the Agency's need for this information, the accuracy of the provided burden estimates, and any suggested methods for minimizing respondent burden, including through the use of automated collection techniques to the Director, Collection Strategies Division, U.S. Environmental Protection Agency (2822T), 1200 Pennsylvania Ave., NW, Washington, D.C. 20460. Include the OMB control number in any correspondence. Do not send the completed EPA Form 7710-25 to this address.

CERTIFICATION -- A printed copy of this signature page, with original signature, must be submitted with CD or paper submission.

I hereby certify to the best of my knowledge and belief that all information entered on this form is complete and accurate. I further certify that, pursuant to 15 U.S.C. § 2613(c), for all claims for protection for any confidential information made with this submission, all information submitted to substantiate such claims is true and correct, and that it is true and correct that the person submitting the claim has:

(i) taken reasonable measures to protect the confidentiality of the information;

(ii) determined that the information is not required to be disclosed or otherwise made available to the public under any other Federal law

(iii) a reasonable basis to conclude that disclosure of the information is likely to cause substantial harm to the competitive position of the person; and

(iv) a reasonable basis to believe that the information is not readily discoverable through reverse engineering.

Any knowing and willful misrepresentation is subject to criminal penalty pursuant to 18 U.S.C. § 1001.

Additional Certification Statements:

If you are submitting a PMN, SNUN, LoREX, LVE, or TMEA, check the following Fees Certification statement that applies:

- ☐ The Company named in Part I, Section A is a "small business concern" as defined under 40 CFR 700.43 and will remit the fee as specified in 40 CFR 700.45(c).
- ☒ The Company named in Part I, Section A will remit the fee as specified in 40 CFR 700.45(c).
- ☐ This joint submission includes at least one Company which is a "small business concern" and at least one Company which is not a "small business concern," as defined under 40 CFR 700.43. The fee will be remitted with the joint submission. Any remaining balance due for this joint submission is to be paid by the secondary submitter(s).
- ☐ The company named in Part I, Section A is submitting a sustainable futures TME. The company has graduated from EPA's Sustainable Futures program and is therefore exempt from fees for this sustainable futures TME.

If you are submitting a **Low Volume Exemption (LVE)** application in accordance with 40 CFR 723.50(c)(1) or a **Low Release and Low Exposure Exemption (LoRex)** application in accordance with 40 CFR 723.50(c)(2), check the following certification statements:

- ☐ The manufacturer submitting this notice intends to manufacture or import the new chemical substance for commercial purposes, other than in small quantities solely for research and development, under the terms of 40 CFR 723.50.
- ☐ The manufacturer is familiar with the terms of this section and will comply with those terms; and
- ☐ The new chemical substance for which the notice is submitted meets all applicable exemption conditions.
- ☐ If this application is for an LVE in accordance with 40 CFR 723.50(c)(1), the manufacturer intends to commence manufacture of the exempted substance for commercial purposes within 1 year of the date of the expiration of the 30 day review period.

				Confidential
Signature and title of Authorized Official (Original Signature Required)	*XXX*	Date	XXX	☒

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Part I -- GENERAL INFORMATION

Section A – SUBMITTER IDENTIFICATION

Mark (X) the "Confidential" box next to any subsection you claim as confidential

1a.	Person Submitting Notice (in U.S.)					Confidential
Name of Authorized Official	(first) XXX		(last) XXX			X
Position	XXX					
Company	XXX					
Mailing Address (number & street)	XXX					
City		State		Postal Code	XXX	
email	XXX					

b.	Agent (if Applicable)					Confidential
Name of Authorized Official	(first)		(last)			☐
Position						
Company						
Mailing Address (number & street)						
City		State		Postal Code		
e-mail		Telephone (include area code)				

c.	Joint Submitter (if applicable)					Confidential
If you are submitting this notice as part of a joint submission, mark (X)					☐	☐
Name of Authorized Official	(first)		(last)			
Position						
Company						
Mailing Address (number & street)						
City		State		Postal Code		
e-mail		Telephone (include area code)				

2.	Technical Contact (in U.S.)					Confidential
Name of Authorized Official	(first) XXX		(last) XXX			X
Position	XXX					
Company	XXX					
Mailing Address (number & street)	XXX					
City	XXX	State	XXX	Postal Code	XXX	
e-mail	XXX	Telephone (include area code)		XXX		

			Mark (X) if none	Confidential
3.	If you have had a prenotice communication (PC) concerning this notice and EPA assigned a PC Number to the notice, enter the number.		X	☐
4.	If you previously submitted an exemption application for the chemical substance covered by this notice, enter the exemption number assigned by EPA. If you previously submitted a PMN for this substance enter the PMN number assigned by EPA (i.e. withdrawn or incomplete).		Mark (X) if none X	Confidential ☐
5.	If you have submitted a notice of Bona fide intent to manufacture or import for the chemical substance covered by this notice, enter the notice number assigned by EPA.		Mark (X) if none X	Confidential ☐

6.	Type of Notice – Mark (X)						
1.	Manufacture Only Binding Option	X ☐	2.	Import Only Binding Option	☐ ☐	3.	Both ☐

Part I – GENERAL INFORMATION -- Continued

Section B – CHEMICAL IDENTITY INFORMATION: You must provide a currently correct Chemical Abstracts (CA) name of the substance based on current CA index nomenclature rules and conventions.

Mark (X) the "Confidential" box next to any item you claim as confidential

Complete either item 1 (Class 1 or 2 substances) or 2 (Polymers) as appropriate. Complete all other items.

If another person will submit chemical identity information for you (for either Item 1 or 2), mark (X) the box at the right. Identify the name, company, and address of that person in a continuation sheet. ☐

1. Class 1 or 2 chemical substances (for definitions of class 1 and class 2 substances, see the Instructions Manual)	Class 1	Class 2	CBI
a. Class of substance - Mark (X)	☐	☐	X

b. Chemical name (Currently correct Chemical Abstracts (CA) Name that is consistent with TSCA Inventory listings for similar substances. For Class 1 substances a CA Index Name must be provided. For Class 2 substances either a CA Index Name or CA Preferred Name must be provided, which ever is appropriate based on current CA index nomenclature rules and conventions). X

XXX

CAS Registry Number (if a number already exists for the substance): XXX

c. Please identify which method you used to develop or obtain the specified chemical identity information reported in this notice: (check one).

Method 1 (CAS Inventory Expert Service - a copy of the Identification report obtained from the CAS Inventory Expert Services must be submitted as an attachment to this notice) X

IES Order Number: 439408-1

Method 2 (Other Source) ☐

Enter Attachment filename for Part I, Section B, 1. c.: Sanitized Document: 2 CAS-IES Report_Redacted.pdf X

d. Molecular formula: XXX X

e. For a class 1 substance, provide a complete and correct chemical structure diagram. For a class 2 substance, provide a correct representative or partial chemical structure diagram, as complete as can be known, if one can be reasonably ascertained. X

See Attachment (Sanitized Document: 1 Structure Diagram_Redacte...
)

Enter Attachment filename for Part I, Section B, 1. e. ☐

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For a class 2 substance - (1) List the immediate precursor substances with their respective CAS Registry Numbers. (2) Describe the nature of the reaction or process. (3) Indicate the range of composition and the typical composition (where appropriate).	Confidential

e. (1) List the immediate precursor substance names with their respective CAS Registry Numbers. ☐

Enter Attachment filename for Part I, Section B, 1. e. (1)		☐

e. (2) Describe the nature of the reaction or process. ☐

Enter Attachment filename for Part I, Section B, 1. e. (2)		☐

e. (3) Indicate the range of composition and the typical composition (where appropriate). ☐

Enter Attachment filename for Part I, Section B, 1. e. (3)		☐

Part I -- GENERAL INFORMATION -- Continued

Section B -- CHEMICAL IDENTITY INFORMATION -- Continued

3. Impurities
   (a) - Identify each impurity that may be reasonably anticipated to be present in the chemical substance as manufactured for commercial purpose. Provide the CAS Registry Number if available. If there are unidentified impurities, enter "unidentified."
   (b) - Estimate the maximum weight % of each impurity. If there are unidentified impurities, estimate their total weight %.

Impurity (a)	CAS Registry Number (a)	Maximum Percent % (b)	Confi-dential
XXX	XXX	XXX	X
XXX	XXX	XXX	X

Mark (X) this box if the data continues on the next page. ☐

Enter Attachment filename for Part I, Section B, 3. ☐

4. Synonyms - Enter any chemical synonyms for the new chemical identified in subsection 1 or 2.
XXX

☒

Enter Attachment filename for Part I, Section B, 4. ☐

5. Trade identification - List trade names for the new chemical substance identified in subsection 1 or 2.
XXX

☒

Enter Attachment filename for Part I, Section B, 5. ☐

6. Generic chemical name - If you claim chemical identify as confidential, you must provide a generic name for your substance that reveals the specific chemical identity of the new chemical substance to the maximum extent possible. Refer to the TSCA Chemical Substance Inventory, 1985 Edition, Appendix B for guidance on developing generic names.

Perfluorodioxaalkanoyl fluoride,

Enter Attachment filename for Part I, Section B, 6.

7. Byproducts - Describe any byproducts resulting from the manufacture, processing, use, or disposal of the new chemical substance. Provide the CAS Registry Number if available.

Byproduct (1)	CAS Registry Number (2)	Confi-dential

Mark (X) this box if the data continues on the next page. ☐

Part I -- GENERAL INFORMATION – Continued

Section B -- CHEMICAL IDENTITY INFORMATION -- Continued

2. Polymers (For a definition of polymer, see the Instructions Manual.)

Confidential

a. Indicate the number-average weight of the lowest molecular weight composition of the polymer you intend to manufacture. Indicate maximum weight percent of low molecular weight species (not including residual monomers, reactants, or solvents) below 500 and below 1,000 absolute molecular weight of that composition. ☐

Describe the methods of measurement or the basis for your estimates:

GPC ☐ | **Other** (Specify Below) ☐

Specify Other:

(i) lowest number average molecular weight:	(ii) maximum weight % below 500 molecular weight:	(iii) maximum weight % below 1000 molecular weight:

Enter Attachment filename for Part I, Section B, 2. a. ☐

b. You must make separate confidentiality claims for monomer or other reactant identity, composition information, and residual information. Mark (X) the "Confidential" box next to any item you claim as confidential

(1) - Provide the specific chemical name and CAS Registry Number (if a number exists) of each monomer or other reactant used in the manufacture of the polymer.
(2) - Mark (X) this column if entry in column (1) is confidential.
(3) - Indicate the typical weight percent of each monomer or other reactant in the polymer.
(4) - Choose "yes" from drop down menu if you want a monomer or other reactant used at two weight percent or less to be listed as part of the polymer description on the TSCA Chemical Substance Inventory.
(5) - Mark (X) this column if entries in columns (3) and (4) are confidential.
(6) - Indicate the maximum weight percent of each monomer or other reactant that may be present as a residual in the polymer as manufactured for commercial purposes.
(7) - Mark (X) this column if entry in column (6) is confidential.

Monomer or other reactant specific chemical name (**1**)	CBI (**2**)	Typical composition (**3**)	Include in identity (**4**)	CBI (**5**)	Max residual (**6**)	CBI (**7**)
CAS Registry Number (**1**)						
CAS Registry Number (**1**)						
CAS Registry Number (**1**)						
CAS Registry Number (**1**)						
CAS Registry Number (**1**)						

Mark (X) this box if the data continues on the next page. ☐

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c. Please identify which method you used to develop or obtain the specified chemical identity information reported in this notice (check one).				CBI
Method 1 (CAS Inventory Expert Service - a copy of the identification report obtained from CAS Inventory Expert Service must be submitted as an attachment to this notice) ☐	IES Order Number		**Method 2** (other source) ☐	
Enter Attachment filename for Part I, Section B, 2. c.				☐

d. The currently correct Chemical Abstracts (CA) name for the polymer that is consistent with TSCA Inventory listings for similar polymers.	☐

CAS Registry Number (if a number already exists for the substance)		

e. Provide a correct representative or partial chemical structure diagram, as complete as can be known, if one can be reasonably ascertained.	☐

Enter Attachment filename for Part I, Section B, 2. e.		☐

Part I -- GENERAL INFORMATION -- Continued

Section C -- PRODUCTION, IMPORT, AND USE INFORMATION:

The information on this page refers to consolidated chemical number(s): [X] **1** [ ] **2** [ ] **3** [ ] **4** [ ] **5** [ ] **6**

Mark (X) the "Confidential" box next to any item you claim as confidential.

1. Production volume -- Estimate the **maximum** production volume during the first 12 months of production. Also estimate the maximum production volume for any consecutive 12-month period during the first three years of production. Estimates should be on 100% new chemical substance basis. For a Low Volume Exemption application, if you choose to have your notice reviewed at a lower production volume than 10,000 kg/yr, specify the volume and mark (x) in the binding box. If granted, you are bound to this volume.

Maximum first 12-month production (kg/yr) (100% new chemical substance basis)	Maximum 12-month production (kg/yr) (100% new chemical substance basis)	Confidential	Binding Option Mark (X)
XXX	XXX	[X]	[ ]

Enter Attachment filename for Part I, Section C, 1.		CBI [ ]

2. Use Information -- You must make separate confidentiality claims for the description of the category of use, the percent of production volume devoted to each category, the formulation of the new substance, and other use information. Mark (X) the "Confidential" Box next to any item you claim as confidential.

a. (1) --Describe each intended category of use of the new chemical substance by function and application.
(2) --Mark (X) this column if entry column (1) is confidential business information (CBI).
(3) --Indicate your willingness to have the information provided in column (1) binding.
(4) --Estimate the percent of total production for the first three years devoted to each category of use.
(5) --Mark (X) this column if entry in column (4) is confidential business information (CBI).
(6) --Estimate the percent of the new substance as formulated in mixtures, suspensions, emulsions, solutions, or gels as manufactured for commercial purposes at sites under your control associated with each category of use.
(7) --Mark (X) this column if entry in column (6) is confidential business information (CBI).
(8) --Indicate % of product volume expected for the listed "use" sectors. Mark more than one box if appropriate. Mark (X) to indicate your willingness to have the use type provided in (8) binding.
(9) --Mark (X) this column if entry(ies) in column (8) is (are) confidential business information (CBI).

Category of use (**1**) (by function and application i.e. a dispersive dye for finishing polyester fibers)	CBI (**2**)	Binding Option Mark (X) (**3**)	Production % (**4**)	CBI (**5**)	% in Formulation (**6**)	CBI (**7**)	% of substance expected per use (**8**)					CBI (**9**)
							Site-limited	Consumer*	Industrial	Commercial	Binding Option	
XXX	X		XXX	X	XXX	X	XXX	XXX	XXX	XXX		X

* If you have identified a "consumer" use, please provide on a continuation sheet a detailed description of the use(s) of this chemical substance in consumer products. In addition include estimates of the concentration of the new chemical substance as expected in consumer products and describe the chemical reactions by which this substance loses its identity in the consumer product.

Mark (X) this box if the data continues on the next page. [ ]

b. Generic use description — If you claim any category of use description in subsection 2a as confidential, enter a generic description of that category. Read the Instruction Manual for examples of generic use descriptions.

Intermediate

Enter Attachment filename for Part I, Section C, 2. b.		CBI [ ]

3. Hazard Information -- Include in the notice a copy of reasonable facsimile of any hazard warning statement, label, material safety data sheet, or other information which will be provided to any person who is reasonably likely to be exposed to this substance regarding protective equipment or practices for the safe handing, transport, use, or disposal of the new substance. List in part III hazard information you include.

Mark (X) this box if you attach hazard information.	[X]	Binding Option Mark (X) [ ]

Part II-- HUMAN EXPOSURE AND ENVIRONMENTAL RELEASE

Section A -- INDUSTRIAL SITES CONTROLLED BY THE SUBMITTER

Mark (X) the "Confidential" box next to any item you claim as confidential

The information on pages 8 and 8a refer to consolidated chemical number(s): [X] **1** [ ] **2** [ ] **3** [ ] **4** [ ] **5** [ ] **6**

Complete section A for each type of manufacture, processing, or use operation involving the new chemical substance at industrial sites you control. Importers do not have to complete this section for operations outside the U.S.; however, you may still have reporting requirements if there are further industrial processing or use operations after import. You must describe these operations. See instructions manual

1. Operation description
   a. Identity -- Enter the identity of the site at which the operation will occur.

				Confi-dential
Name	XXX			
Site address (number and street)	XXX			[X]
City	XXX	County	XXX	
State	XXX	ZIP code	XXX	

If the same operation will occur at more than one site, enter the number of sites. Identify the additional sites on a continuation sheet, and if any of the sites have significantly different production rates or operations, include all the information requested in this section for those sites as attachments. →	XXX	[X]
Mark (X) this box if the data continues on the next page.	[ ]	

b. Type -- Mark (X) Manufacturing [ ] Processing [ ] Use [ ] — [X]

c. Amount and Duration -- Complete 1 or 2 as appropriate

				Confi-dential
1. Batch	Maximum kg/batch (100% new chemical substance)	Hours/batch	Batches/year	[ ]
2. Continuous	Maximum kg/day (100% new chemical substance)	Hours/day	Days/year	[X]
	XXX	XXX	XXX	

d. Process description — Mark (X) to indicate your willingness to have your process description binding. → [ ]

(1) Diagram the major unit operation steps and chemical conversions. Include interim storage and transport containers (specify- e.g. 5 gallon pails, 55 gallon drum, rail car, tank truck, etc.).
(2) Provide the identity, the approximate weight (by kg/day or kg/batch on a 100% new chemical substance basis), and entry point of all starting materials and feedstocks (including reactants, solvents, catalysts, etc.), and of all products, recycle streams, and wastes. Include cleaning chemicals (note frequency if not used daily or per batch.).
(3) Identify by number the points of release, including small or intermittent releases, to the environment of the new chemical substance. If releasing to two media at the same step, assign a second release number for the second medium.

[X]

XXX

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Diagram of the major unit operation steps.	Confidential
	X

See Attachment (Sanitized Document: 4 Process Diagram_Substance...
)

Enter Attachment filename for Part II, Section A, 1. d.	Sanitized Document: 4 Process Diagram_Substance... X

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Part II-- HUMAN EXPOSURE AND ENVIRONMENTAL RELEASE -- Continued

Section A -- INDUSTRIAL SITES CONTROLLED BY THE SUBMITTER -- Continued

The information on pages 9 and 9a refer to consolidated chemical number(s): [X] **1** [ ] **2** [ ] **3** [ ] **4** [ ] **5** [ ] **6**

2. Occupational Exposure -- You must make separate confidentiality claims for the description of worker activity, physical form of the new chemical substance, number of workers exposed, and duration of activity. Mark (X) the "Confidential" box next to any item you claim as confidential.

(1) -- Describe the activities (i.e. bag dumping, tote filling, unloading drums, sampling, cleaning, etc.) in which workers may be exposed to the substance.
(2) -- Mark (X) this column if entry in column (1) is confidential business information (CBI).
(3) -- Describe any protective equipment and engineering controls used to protect workers.
(4) and (6) -- Indicate your willingness to have the information provided in column (3) or (5) binding.
(5) -- Indicate the physical form(s) of the new chemical substance (e.g., solid: crystal, granule, powder, or dust) and % new chemical substance (if part of a mixture) at the time of exposure.
(7) -- Mark (X) this column if entries in columns (3) and (5) are confidential business information (CBI).
(8) -- Estimate the maximum number of workers involved in each activity for all sites combined.
(9) -- Mark (X) this column if entry in column (8) is confidential business information (CBI).
(10) and (11) -- Estimate the maximum duration of the activity for any worker in hours per day and days per year.
(12) -- Mark (X) this column if entries in columns (10) and (11) are confidential business information (CBI).

Worker activity (i.e., bag dumping, filling drums) (1)	CBI (2)	Protective Equipment/ Engineering Controls (3)	Binding Option Mark (X) (4)	Physical form(s) & % new substance (5)	Binding Option Mark (X) (6)	CBI (7)	# of Workers Exposed (8)	CBI (9)	Maximum Duration		CBI (12)
									Hrs/Day (10)	Days/Yr (11)	
XXX	X	XXX		XXX		X	XXX	X	XXX	XXX	X
XXX	X	XXX		XXX		X	XXX	X	XXX	XXX	X

Mark (X) this box if the data continues on the next page. [ ]

Enter Attachment filename for Part II, Section A on the bottom of page 9a. [ ]

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3. Environmental Release and Disposal -- You must make separate confidentiality claims for the release number and the amount of the new chemical substance released and other release and disposal information. Mark (X) the "Confidential" box next to each item you claim as confidential.

(1) -- Enter the number of each release point identified in the process description, part II, section A, subsection 1d(3).
(2) -- Estimate the amount of the new substance released (a) directly to the environment or (b) into control technology (in kg/day or kg/batch).
(3) -- Mark (X) this column if entries in columns (1) and (2) are confidential business information (CBI).
(4) -- Identify the media (stack air, fugitive air (optional-see Instruction Manual), surface water, on-site or off-site land or incineration, POTW, or other (specify)) to which the new substance will be released from that release point.
(5) -- a. Describe control technology, if any, and control efficiency that will be used to limit the release of the new substance to the environment. For releases disposed of on land, characterize the disposal method and state whether it is approved for disposal of RCRA hazardous waste. On a continuation sheet, for each site describe any additional disposal methods that will be used and whether the waste is subject to secondary or tertiary on-site treatment. b. Estimate the amount released to the environment after control technology (in kg/day).
(6) -- Mark (X) this column if entries in columns (4) and (5) are confidential business information (CBI).
(7) -- Identify the destination(s) of releases to water. Please supply NPDES (National Pollutant Discharge Elimination System) numbers for direct discharges or NPDES numbers of the POTW (Publicly Owned Treatment Works). Mark (X) if the POTW name or NPDES # is confidential business information (CBI).

Release Number	Amount of New Substance Released		CBI	Medium of release e.g. Stack air	Control technology and efficiency (you may wish to optionally attach efficiency data)			CBI
(1)	(2a)	(2b)	(3)	(4)	(5a)	Binding Mark (X)	(5b)	(6)
XXX	XXX	XXX	X	XXX	XXX		XXX	X
XXX	XXX	XXX	X	XXX	XXX		XXX	X
XXX	XXX	XXX	X	XXX	XXX		XXX	X
Mark (X) this box if the data continues on the next page.							☐	

(7) Mark (X) the destination(s) of releases to water.		NPDES#	CBI
☐ POTW--provide name(s)			☐
☐ Navigable waterway- - provide name(s)			☐
☐ Other--Specify			☐
Enter Attachment filename for Part II, Section A.			☐

Part II-- HUMAN EXPOSURE AND ENVIRONMENTAL RELEASE – Continued

Section B -- INDUSTRIAL SITES CONTROLLED BY OTHERS

The information on pages 10 and 10a refer to consolidated chemical number(s): ☐ **1** ☐ **2** ☐ **3** ☐ **4** ☐ **5** ☐ **6**

Complete section B for typical processing or use operations involving the new chemical substance at sites you do not control. Importers do not have to complete this section for operations outside the U.S.; however, you must report any processing or use activities after import. See the Instructions Manual. *Complete a separate section B for each type of processing, or use operation involving the new chemical substance*. If the same operation is performed at more than one site describe the typical operation common to these sites. Identify additional sites on a continuation sheet.

1(a). Operation Description -- To claim information in this section as confidential, bracket (e.g. {}) the specific information that you claim as confidential.

(1) -- Diagram the major unit operation steps and chemical conversions, including interim storage and transport containers (specify - e.g. 5 gallon pails, 55 gallon drums, rail cars, tank trucks, etc). On the diagram, identify by letter and briefly describe each worker activity.

(2) -- Either in the diagram or in the text field 1(b) below, provide the identity, the approximate weight (by kg/day or kg/batch, on an 100% new chemical substance basis), and entry point of all feedstocks (including reactants, solvents and catalysts, etc) and all products, recycle streams, and wastes. Include cleaning chemicals (note frequency if not used daily or per batch).

(3) -- Either in the diagram or in the text field 1(b) below, identify by number the points of release, including small or intermittent releases, to the environment of the new chemical substance.

(4) -- Please enter the # of sites (remember to identify the locations of these sites on a continuation sheet):

	Number of Sites		Confidential ☐

1(b). (Optional) This space is for a text description to clarify the diagram above. Confidential ☐

Enter Attachment filename for Part II, Section B on the bottom of page 10a.		☐

PMN Page 10a

2. Worker Exposure/Environmental Release

(1) -- From the diagram above, provide the letter for each worker activity. Complete 2-8 for each worker activity described.
(2) -- Estimate the number of workers exposed for all sites combined.
(4) -- Estimate the typical duration of exposure per worker in (a) hours per day and (b) days per year.
(6) -- Describe physical form of exposure and % new chemical substance (if in mixture), and any protective equipment and engineering controls, if any, used to protect workers.
(7) -- Estimate the percent of the new substance as formulated when packaged or used as a final product.
(9) -- From the process diagram above, enter the number of each release point. Complete 9-13 for each release point identified.
(10) -- Estimate the amount of the new substance released (a) directly to the environment or (b) into control technology to the environment (in kg/day or kg/batch).
(12) -- Describe media of release i.e. stack air, fugitive air (optional-see Instructions Manual), surface water, on-site or off-site land or incineration, POTW, or other (specify) and control technology, if any, that will be used to limit the release of the new substance to the environment.
(14) -- Identify byproducts which may result from the operation.
(3), (5), (8), (11), (13) and (15) -- Mark (X) this column if any of the proceeding entries are confidential business information (CBI).

Letter of Activity	# of Workers Exposed	CBI	Duration of Exposure		CBI	Protective Equip./Engineering Controls/Physical Form	% new substance	% in Formulation	CBI
(1)	(2)	(3)	(4a)	(4b)	(5)	(6)	(6)	(7)	(8)

Release Number	Amount of New Substance Released		CBI	Media of Release & Control Technology	CBI
(9)	(10a)	(10b)	(11)	(12)	(13)

Mark (X) this box if the data continues on the next page. ☐

(14) Byproducts: | **(15) CBI** ☐

Enter Attachment filename for Part II, Section B. ☐

OPTIONAL POLLUTION PREVENTION INFORMATION

To claim information in the following section as confidential, bracket (e.g. {}) the specific information that you claim as confidential.

In this section you may provide information not reported elsewhere in this form regarding your efforts to reduce or minimize potential risks associated with activities surrounding manufacturing, processing, use and disposal of the PMN substance. Please include new information pertinent to pollution prevention, including source reduction, recycling activities and safer processes or products available due to the new chemical substance. Source reduction includes the reduction in the amount or toxicity of chemical wastes by technological modification, process and procedure modification, product reformulation, and/or raw materials substitution. Recycling refers to the reclamation of useful chemical components from wastes that would otherwise be treated or released as air emissions or water discharges, or land disposal. Quantitative or qualitative descriptions of pollution prevention, source reduction and recycling should emphasize potential risk reduction in addition to compliance with existing regulatory requirements. The EPA is interested in the information to assess overall net reductions in toxicity or environmental releases and exposures, not the shifting of risks to other media (e.g., air to water) or nonenvironmental areas (e.g., occupational or consumer exposure). To the extent known, information about the technology being replaced will assist EPA in its relative risk determination. In addition, information on the relative cost or performance characteristics of the PMN substance to potential alternatives may be provided.

Describe the expected net benefits, such as

(1) an overall reduction in risk to human health or the environment;
(2) a reduction in the generation of waste materials through recycling, source reduction or other means;
(3) a reduction in the use of hazardous starting materials, reagents, or feedstocks;
(4) a reduction in potential toxicity, human exposure and/or environmental release; or
(5) the extent to which the new chemical substance may be a substitute for an existing substance that poses a greater overall risk to human health or the environment.

Information provided in this section will be taken into consideration during the review of this substance. See PMN Instructions Manual and Pollution Prevention Guidance manual for guidance and examples.

XXX

Enter Attachment filename for Pollution Prevention Page 11.		☐

Part III -- LIST OF ATTACHMENTS

Attach continuation sheets for sections of the form, test data and other data (including physical/chemical properties and structure/activity information), and optional information after this page. Clearly identify the attachment and the section of the form to which it relates, if appropriate. Number consecutively the pages of any paper attachments. In the Number of Pages column below, enter the inclusive page numbers of each attachment for paper submissions or enter the total number of pages for each attachment for electronic submissions. Electronic attachments can be identified by filename.
Mark (X) the "Confidential" box next to any attachment name or filename you claim as confidential. Read the Instructions Manual for guidance on how to claim any information in an attachment as confidential. You must include with the sanitized copy of the notice form a sanitized version of any attachment in which you claim information as confidential.

#	Attachment Name	Attachment Filename	Number of Pages	Associated PMN Section Number	CBI
1	SDS	SDS_1 _Redacted.pdf	13	Hazard Information Section (Chemical 869200)	
2	Physical Chemical Property Reports	Physical Chemical Properties_Redacted.pdf	84	Physical and Chemical Properties Worksheet Continued (Chemical	
3	Structure	Structure Diagram_Redacted.pdf	1	Class 1 or 2 Substances Chemical Structure Diagram (Chemical	
4	IES Report	CAS-IES Report_Redacted.pdf	1	Class 1 or 2 Substances ID Method (Chemical 869200)	
5	Process Diagram	Process Diagram_Substance 1 _Redacted.pdf	1	Submitter Controlled Operations (Operation 1)	
6	Acute Inhalation Study	Acute Inhalation_Redacted.pdf	2	Additional Attachments	
7	AMES	AMES_Redacted.pdf	48	Additional Attachments	

Mark (X) this box if the data continues on the next page. ☐

PMN Page 13

PHYSICAL AND CHEMICAL PROPERTIES WORKSHEET

The information on this page refers to chemical number(s): [X] 1 [ ] 2 [ ] 3 [ ] 4 [ ] 5 [ ] 6

To assist EPA's review of physical and chemical properties data, please complete the following worksheet for data you provide and include it in the notice. Identify the property measured, the value of the property, the units in which the property is measured (as necessary), and whether or not the property is claimed as confidential. Give the attachment number (found on page 12) in column (b). The physical state of the neat substance should be provided. These measured properties should be for the neat (100% pure) chemical substance. Properties that are measured for mixtures or formulations should be so noted (% PMN substance in __). You are not required to submit this worksheet; however, EPA strongly recommends that you do so, as it will simplify the review and ensure that confidential information is properly protected. You should submit this worksheet as a supplement to your submission of test data. This worksheet is not a substitute for submission of test data.

Property (a)		Unit	Mark X if Provided	Attachment Number (b)	Value (c)			Measured or Estimate (M or E)	CBI Mark (X) (d)
Physical state of neat substance			[ ]		(solid) [ ]	(liquid) [ ]	(gas) [ ]		
Vapor Pressure @ Temperature		°C	[ ]				Torr		
Density/relative density			[ ]				g/cm3		
Solubility			[ ]				g/L		
@ Temperature		°C							
Solvent									
Solubility in Water @ Temperature	XXX	°C	[X]	XXX	XXX		g/L	XXX	X
Melting Temperature			[X]	XXX	XXX		°C	XXX	X
Boiling / Sublimation temperature @		Torr	[ ]				°C		
Spectra			[ ]						
Dissociation constant			[ ]						
Octanol / water partition coefficient			[X]	XXX	XXX			XXX	X
Henry's Law constant			[ ]						
Volatilization from water			[ ]						
Volatilization from soil			[ ]						
pH@ concentration			[ ]						
Flammability			[ ]						
Explodability			[ ]						
Adsorption / Coefficient			[ ]						
Particle Size Distribution			[ ]						
Other – Specify	XXX		[X]	XXX	XXX			XXX	X

Continuation Sheet

ID		Field	

PHYSICAL AND CHEMICAL PROPERTIES WORKSHEET

Property (a)		Mark X if Provided	Attachment Number (b)	Value (c)	Measured or Estimate (M or E)	CBI Mark (X) (d)
Other – Specify	XXX	☒	XXX	XXX	XXX	X
Other – Specify		☐				
Other – Specify		☐				
Other – Specify		☐				
Other – Specify		☐				
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Other – Specify		☐				
Other – Specify		☐				

CAS
A DIVISION OF THE
AMERICAN CHEMICAL SOCIETY

InventoryExpertService

Phone: 800-631-1884, 614-447-3870
Fax: 614-447-3747
E-mail: answers@cas.org
Web: cas.org/services/knowledge

INVENTORY EXPERT SERVICE REPORT

Please print the above CA Index Name on the appropriate page of your PMN.

☐ If this box is checked, CAS has made correction(s) marked in red to your IES order. Please make the same corrections to your PMN before submitting it to the EPA.

Recommended use of the chemical and restrictions on use

Recommended use	:	Scientific research and development
Restrictions on use	:	For professional users only., This product is for experimental uses only. The product has not been completely analyzed and all of the hazards may not be known. Please use caution while handling this product.

SECTION 2. HAZARDS IDENTIFICATION

GHS classification in accordance with 29 CFR 1910.1200

Acute toxicity (Inhalation)	:	Category 2

GHS label elements

Hazard pictograms	:	
Signal Word	:	Danger
Hazard Statements	:	H330 Fatal if inhaled.
Precautionary Statements	:	**Prevention:** P260 Do not breathe mist or vapors. P271 Use only outdoors or in a well-ventilated area. P284 Wear respiratory protection. **Response:**

P304 + P340 + P310 IF INHALED: Remove person to fresh air and keep comfortable for breathing. Immediately call a POISON CENTER/doctor.

Storage:

P405 Store locked up.

Disposal:

P501 Dispose of contents/ container to an approved waste disposal plant.

Other hazards

None known.

SECTION 4. FIRST AID MEASURES

General advice	:	In the case of accident or if you feel unwell, seek medical advice immediately. When symptoms persist or in all cases of doubt seek medical advice.
If inhaled	:	If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention immediately.
In case of skin contact	:	Wash with water and soap as a precaution. Get medical attention if symptoms occur.
In case of eye contact	:	Flush eyes with water as a precaution. Get medical attention if irritation develops and persists.
If swallowed	:	If swallowed, DO NOT induce vomiting. Get medical attention if symptoms occur. Rinse mouth thoroughly with water.
Most important symptoms and effects, both acute and delayed	:	Fatal if inhaled.

Protection of first-aiders	:	First Aid responders should pay attention to self-protection, and use the recommended personal protective equipment when the potential for exposure exists (see section 8).
Notes to physician	:	Treat symptomatically and supportively.

SECTION 5. FIRE-FIGHTING MEASURES

Suitable extinguishing media	:	Water spray Alcohol-resistant foam Carbon dioxide (CO2) Dry chemical
Unsuitable extinguishing media	:	None known.
Specific hazards during fire fighting	:	Exposure to combustion products may be a hazard to health.
Hazardous combustion products	:	Hydrogen fluoride carbonyl fluoride potentially toxic fluorinated compounds aerosolized particulates Carbon oxides
Specific extinguishing methods	:	Use extinguishing measures that are appropriate to local circumstances and the surrounding environment. Use water spray to cool unopened containers. Remove undamaged containers from fire area if it is safe to do so. Evacuate area.
Special protective equipment for fire-fighters	:	In the event of fire, wear self-contained breathing apparatus. Use personal protective equipment.

SECTION 6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures	:	Evacuate personnel to safe areas. Only trained personnel should re-enter the area. Follow safe handling advice and personal protective equipment recommendations.
Environmental precautions	:	Discharge into the environment must be avoided. Prevent further leakage or spillage if safe to do so. Prevent spreading over a wide area (e.g., by containment or oil barriers). Retain and dispose of contaminated wash water. Local authorities should be advised if significant spillages cannot be contained.
Methods and materials for	:	Soak up with inert absorbent material.

containment and cleaning up	For large spills, provide diking or other appropriate containment to keep material from spreading. If diked material can be pumped, store recovered material in appropriate container. Clean up remaining materials from spill with suitable absorbent. Local or national regulations may apply to releases and disposal of this material, as well as those materials and items employed in the cleanup of releases. You will need to determine which regulations are applicable. Sections 13 and 15 of this SDS provide information regarding certain local or national requirements.

SECTION 7. HANDLING AND STORAGE

Technical measures	:	See Engineering measures under EXPOSURE CONTROLS/PERSONAL PROTECTION section.
Local/Total ventilation	:	If sufficient ventilation is unavailable, use with local exhaust ventilation.
Advice on safe handling	:	Do not breathe vapors or spray mist. Do not swallow. Avoid contact with eyes. Avoid prolonged or repeated contact with skin. Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment Keep container tightly closed. Keep away from water. Protect from moisture. Take care to prevent spills, waste and minimize release to the environment.
Conditions for safe storage	:	Keep in properly labeled containers. Store locked up. Keep tightly closed. Keep in a cool, well-ventilated place. Store in accordance with the particular national regulations.
Materials to avoid	:	Do not store with the following product types: Strong oxidizing agents Flammable liquids Flammable solids Pyrophoric liquids Pyrophoric solids Self-heating substances and mixtures Substances and mixtures which in contact with water emit flammable gases Explosives Gases

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Ingredients with workplace control parameters

Contains no substances with occupational exposure limit values.

Occupational exposure limits of decomposition products

Components	CAS-No.	Value type (Form of exposure)	Control parameters / Permissible concentration	Basis
Hydrofluoric acid	7664-39-3	TWA	3 ppm 2.5 mg/m³	NIOSH REL
		C	6 ppm 5 mg/m³	NIOSH REL
		TWA	3 ppm	OSHA Z-2
		TWA	0.5 ppm (Fluorine)	ACGIH
		C	2 ppm (Fluorine)	ACGIH
Carbonyl difluoride	353-50-4	TWA	2 ppm	ACGIH
		STEL	5 ppm	ACGIH
		ST	5 ppm 15 mg/m³	NIOSH REL
		TWA	2 ppm 5 mg/m³	NIOSH REL
Carbon dioxide	124-38-9	TWA	5,000 ppm	ACGIH
		STEL	30,000 ppm	ACGIH
		TWA	5,000 ppm 9,000 mg/m³	OSHA Z-1
		TWA	5,000 ppm 9,000 mg/m³	NIOSH REL
		ST	30,000 ppm 54,000 mg/m³	NIOSH REL
Carbon monoxide	630-08-0	TWA	25 ppm	ACGIH
		TWA	35 ppm 40 mg/m³	NIOSH REL
		C	200 ppm 229 mg/m³	NIOSH REL
		TWA	50 ppm 55 mg/m³	OSHA Z-1

Engineering measures : Processing may form hazardous compounds (see section 10).
Minimize workplace exposure concentrations.
If sufficient ventilation is unavailable, use with local exhaust ventilation.

Personal protective equipment

Respiratory protection	:	General and local exhaust ventilation is recommended to maintain vapor exposures below recommended limits. Where concentrations are above recommended limits or are unknown, appropriate respiratory protection should be worn. Follow OSHA respirator regulations (29 CFR 1910.134) and use NIOSH/MSHA approved respirators. Protection provided by air purifying respirators against exposure to any hazardous chemical is limited. Use a positive pressure air supplied respirator if there is any potential for uncontrolled release, exposure levels are unknown, or any other circumstance where air purifying respirators may not provide adequate protection.
Hand protection		
Material	:	Chemical-resistant gloves
Remarks	:	Choose gloves to protect hands against chemicals depending on the concentration specific to place of work. Breakthrough time is not determined for the product. Change gloves often! For special applications, we recommend clarifying the resistance to chemicals of the aforementioned protective gloves with the glove manufacturer. Wash hands before breaks and at the end of workday.
Eye protection	:	Wear the following personal protective equipment: Safety glasses
Skin and body protection	:	Skin should be washed after contact.
Hygiene measures	:	If exposure to chemical is likely during typical use, provide eye flushing systems and safety showers close to the working place. When using do not eat, drink or smoke. Wash contaminated clothing before re-use.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance	:	liquid
Color	:	No data available
Odor	:	No data available
Odor Threshold	:	No data available
pH	:	No data available

Melting point/freezing point	:	No data available
Initial boiling point and boiling range	:	
Flash point	:	does not flash
Evaporation rate	:	No data available
Flammability (solid, gas)	:	Not applicable
Flammability (liquids)	:	No data available
Upper explosion limit / Upper flammability limit	:	No data available
Lower explosion limit / Lower flammability limit	:	No data available
Vapor pressure	:	No data available
Relative vapor density	:	No data available
Relative density	:	No data available
Solubility(ies)		
Water solubility	:	No data available
Partition coefficient: n-octanol/water	:	No data available
Autoignition temperature	:	No data available
Decomposition temperature	:	No data available
Viscosity		
Viscosity, kinematic	:	No data available
Explosive properties	:	Not explosive
Oxidizing properties	:	The substance or mixture is not classified as oxidizing.
Particle size	:	Not applicable

SECTION 10. STABILITY AND REACTIVITY

Reactivity	:	Not classified as a reactivity hazard.
Chemical stability	:	Stable under normal conditions.
Possibility of hazardous reactions	:	Can react with strong oxidizing agents. Hazardous decomposition products will be formed upon

contact with water or humid air.
Hazardous decomposition products will be formed at elevated temperatures.

Conditions to avoid : Exposure to moisture.

Incompatible materials : Oxidizing agents
Water

Hazardous decomposition products

Contact with water or humid air : Hydrofluoric acid

Thermal decomposition : Carbonyl difluoride
Carbon dioxide
Carbon monoxide

SECTION 11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure

Inhalation
Skin contact
Ingestion
Eye contact

Acute toxicity

Fatal if inhaled.

Product:

Acute inhalation toxicity : Acute toxicity estimate: 235 ppm
Exposure time: 4 h
Test atmosphere: gas
Method: Calculation method

Components:

Acute inhalation toxicity : LC50 (Rat): 235 ppm
Exposure time: 4 h
Test atmosphere: gas
Method: OECD Test Guideline 403

Skin corrosion/irritation

Not classified based on available information.

Serious eye damage/eye irritation

Not classified based on available information.

Respiratory or skin sensitization

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.

Germ cell mutagenicity
Not classified based on available information.

Carcinogenicity
Not classified based on available information.

IARC No ingredient of this product present at levels greater than or equal to 0.1% is identified as probable, possible or confirmed human carcinogen by IARC.

OSHA No component of this product present at levels greater than or equal to 0.1% is on OSHA's list of regulated carcinogens.

NTP No ingredient of this product present at levels greater than or equal to 0.1% is identified as a known or anticipated carcinogen by NTP.

Reproductive toxicity
Not classified based on available information.

STOT-single exposure
Not classified based on available information.

STOT-repeated exposure
Not classified based on available information.

Aspiration toxicity
Not classified based on available information.

SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

Ecotoxicology Assessment

Acute aquatic toxicity	:	Toxic effects cannot be excluded
Chronic aquatic toxicity	:	Toxic effects cannot be excluded

Persistence and degradability
No data available

Bioaccumulative potential
No data available

Mobility in soil

No data available

Other adverse effects

No data available

SECTION 13. DISPOSAL CONSIDERATIONS

Disposal methods

Waste from residues	:	Dispose of in accordance with local regulations.
Contaminated packaging	:	Empty containers should be taken to an approved waste handling site for recycling or disposal. If not otherwise specified: Dispose of as unused product.

SECTION 14. TRANSPORT INFORMATION

International Regulations

UNRTDG

UN number	:	UN 2810
Proper shipping name	:	TOXIC LIQUID, ORGANIC, N.O.S.
Class	:	6.1
Packing group	:	I
Labels	:	6.1

IATA-DGR

UN/ID No.	:	UN 2810
Proper shipping name	:	Toxic liquid, organic, n.o.s.
Class	:	6.1
Packing group	:	I
Labels	:	Toxic
Packing instruction (cargo aircraft)	:	658
Packing instruction (passenger aircraft)	:	652

IMDG-Code

UN number	:	UN 2810
Proper shipping name	:	TOXIC LIQUID, ORGANIC, N.O.S.
Class	:	6.1
Packing group	:	I
Labels	:	6.1
EmS Code	:	F-A, S-A
Marine pollutant	:	no

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code

Not applicable for product as supplied.

Domestic regulation

49 CFR

UN/ID/NA number	:	UN 2810
Proper shipping name	:	Toxic, liquids, organic, n.o.s.
Class	:	6.1
Packing group	:	I
Labels	:	TOXIC
ERG Code	:	153
Marine pollutant	:	no

Special precautions for user

The transport classification(s) provided herein are for informational purposes only, and solely based upon the properties of the unpackaged material as it is described within this Safety Data Sheet. Transportation classifications may vary by mode of transportation, package sizes, and variations in regional or country regulations.

SECTION 15. REGULATORY INFORMATION

EPCRA - Emergency Planning and Community Right-to-Know

CERCLA Reportable Quantity

This material does not contain any components with a CERCLA RQ.

SARA 304 Extremely Hazardous Substances Reportable Quantity

This material does not contain any components with a section 304 EHS RQ.

SARA 302 Extremely Hazardous Substances Threshold Planning Quantity

This material does not contain any components with a section 302 EHS TPQ.

SARA 311/312 Hazards	:	Acute toxicity (any route of exposure)
SARA 313	:	This material does not contain any chemical components with known CAS numbers that exceed the threshold (De Minimis) reporting levels established by SARA Title III, Section 313.

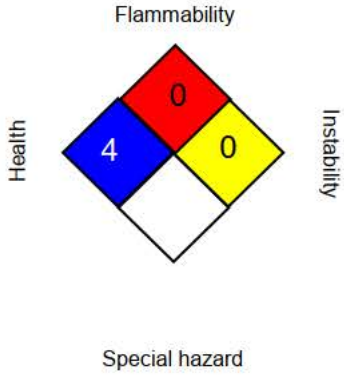
US State Regulations

Pennsylvania Right To Know

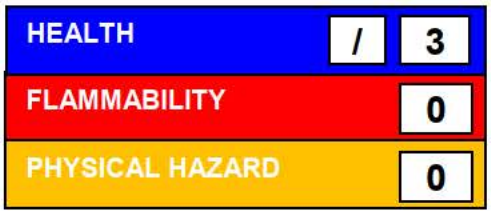
SECTION 16. OTHER INFORMATION

Further information

NFPA 704:



HMIS® IV:



HMIS® ratings are based on a 0-4 rating scale, with 0 representing minimal hazards or risks, and 4 representing significant hazards or risks. The "*" represents a chronic hazard, while the "/" represents the absence of a chronic hazard.

Full text of other abbreviations

ACGIH	:	USA. ACGIH Threshold Limit Values (TLV)
NIOSH REL	:	USA. NIOSH Recommended Exposure Limits
OSHA Z-1	:	USA. Occupational Exposure Limits (OSHA) - Table Z-1 Limits for Air Contaminants
OSHA Z-2	:	USA. Occupational Exposure Limits (OSHA) - Table Z-2
ACGIH / TWA	:	8-hour, time-weighted average
ACGIH / STEL	:	Short-term exposure limit
ACGIH / C	:	Ceiling limit
NIOSH REL / TWA	:	Time-weighted average concentration for up to a 10-hour workday during a 40-hour workweek
NIOSH REL / ST	:	STEL - 15-minute TWA exposure that should not be exceeded at any time during a workday
NIOSH REL / C	:	Ceiling value not be exceeded at any time.
OSHA Z-1 / TWA	:	8-hour time weighted average
OSHA Z-2 / TWA	:	8-hour time weighted average

AICS - Australian Inventory of Chemical Substances; ASTM - American Society for the Testing of Materials; bw - Body weight; CERCLA - Comprehensive Environmental Response, Compensation, and Liability Act; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DOT - Department of Transportation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; EHS - Extremely Hazardous Substance; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; HMIS - Hazardous Materials Identification System; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC

- International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; IMO - International Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International Organisation for Standardization; KECI - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50 % of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; MSHA - Mine Safety and Health Administration; n.o.s. - Not Otherwise Specified; NFPA - National Fire Protection Association; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; RCRA - Resource Conservation and Recovery Act; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; RQ - Reportable Quantity; SADT - Self-Accelerating Decomposition Temperature; SARA - Superfund Amendments and Reauthorization Act; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TSCA - Toxic Substances Control Act (United States); UN - United Nations; UNRTDG - United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bioaccumulative

Sources of key data used to compile the Material Safety Data Sheet	:	Internal technical data, data from raw material SDSs, OECD eChem Portal search results and European Chemicals Agency, http://echa.europa.eu/
Revision Date	:	09/30/2019

The information provided in this Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and shall not be considered a warranty or quality specification of any type. The information provided relates only to the specific material identified at the top of this SDS and may not be valid when the SDS material is used in combination with any other materials or in any process, unless specified in the text. Material users should review the information and recommendations in the specific context of their intended manner of handling, use, processing and storage, including an assessment of the appropriateness of the SDS material in the user's end product, if applicable.

US / Z8

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Copies to: J. Mitchell (6)
W. Wright (1)

ACUTE INHALATION TOXICITY

Procedure: The test material (288 g.) was transferred to a two-inch diameter stainless steel cylinder. A micrometering valve was attached to the main valve and placed inside an upright Multiple Unit Electric Furnace heated to 45°C. Delivery rate of material was controlled with the dual valve system. Stainless steel tubing leading from the cylinder to the top of a 20-liter exposure chamber was wrapped in heating tapes keeping temperatures above 29°C. Chamber air was analyzed by scrubbing it through impingers containing 0.05 N NaOH. Samples were read on a Beckman pH meter equipped with a fluoride specific ion electrode. Results are expressed in micrograms of total ionizable fluoride per liter of air sampled.

Six male ChR-CD rats (initial weight 250-300 grams) were used for each four-hour exposure. Surviving rats were weighed and observed daily for 14 days post-exposure. Animals were chosen at random for pathological examination.

Results:

Concentration in μg F^-/liter	Mortality Ratio
93	0/6
182	1/6
255	Serial sacrifice
433	6/6

Clinical Signs

During Exposure: At lethal concentrations, rats salivated, showed heavy irregular respiration followed by gasping, had corneal opacity and a reddish nasal discharge. Terminal convulsions were seen in a few animals.

At nonlethal levels, respiratory rate increased, rats were pale with reddish eyes.

Post-Exposure: At lethal levels, most animals died during exposure or within 24 hours post-exposure.

At nonlethal levels, rats lost slight to moderate (5-20%) total body weight after 24 hours and then resumed normal weight gain.

Pathology Summary: Nine young adult male ChR-CD rats were divided into three groups. One group of five rats was subjected to a single inhalation exposure of 255 µg F^-/liter of air derived from the fluoride. The second and third groups of two rats each were subjected to the above test compound by single inhalation exposures of 182 and 93 µg F^-/liter respectively. Rats were killed at various intervals of recovery post-exposure.

The gross and microscopic lesions seen were mostly confined to the lung. Hyperplasia of alveolar lining cells and pneumonitis were seen and probably were caused by the test compound. There appears to be a dose-related response in the severity of the lesion, i.e., the higher the concentration of exposure, the more severe the tissue reaction. The effect probably reflects irritation by the test material.

Similar changes can be seen in various chronic inflammations of the lung including verminous pneumonia and toxoplasmosis. Therefore, it is questionable whether the lung lesions were truly test-compound related.*

Summary: The acute lethal concentration by four-hour inhalation exposures of young adult male ChR-CD rats to is equivalent to 182 µg ionizable F^-/liter. With the structural formula and assuming one ionizable fluoride, the fluoride analysis has represented an ALC of 19/248 or 7.66% total compound. Therefore, 182 µg F^-/liter of air would be equivalent to 2375.9 µg compound/liter or 2.38 mg/liter. With a molecular weight of 248, 2.38 mg/liter compound is equal to 2.38 mg/liter x 98.6 ppm/mg/liter or 234.7 ppm. This concentration is considered moderately toxic.

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* Pathology Report #50-74 by R. N. Sharma, D.V.M.

TKB:dhg
Date Issued: August 19, 1974
Report No. 471-74
N.B. E-3313; pp. 56-71.

FINAL REPORT

Study Title

Bacterial Reverse Mutation Assay

Testing Guidelines

OECD Guideline 471, updated and adopted 21 July 1997 and ISO/IEC 17025:2005 (ISO/IEC, 2005)

Test Substance

Author

Emily Dakoulas, BS

Study Completion Date

27 August 2018

Testing Facility

BioReliance Corporation
9630 Medical Center Drive
Rockville, MD 20850

BioReliance Study Number

AF28PN.503.BTL

Sponsor

Sponsor Number

1. STATEMENT OF COMPLIANCE

Study No. AF28PN.503.BTL was conducted in compliance with the following regulation: US EPA GLP Standards 40 CFR 792 (TSCA). This regulation is compatible to non-US regulations, OECD Principles of Good Laboratory Practice (C(97)186/Final); Japanese Ministry of Health, Labor and Welfare Good Laboratory Practices (Ordinance Nos. 21 and 114, if applicable); Japanese Ministry of Agriculture, Forestry and Fisheries Good Laboratory Practices (No. 11 Nousan-6283); Japanese Ministry of Economy, Trade and Industry Good Laboratory Practices, and allows submission of the report under the Mutual Acceptance of Data (MAD) agreement with applicable OECD member countries. The following exceptions were noted:

1. The identity, strength, purity, stability and composition or other characteristics to define the test substance have not been determined.

   Study Director Impact Statement: The impact cannot be determined because the appropriate information was not provided to the Study Director. The study conclusion was based on the test substance as supplied.

2. Analyses to determine the concentration, uniformity and stability of the test substance dose formulations were not performed.

   Study Director Impact Statement: The impact cannot be determined because the appropriate analyses were not performed. The study conclusion was based on the nominal dose levels as documented in the study records.

Emily Dakoulas, BS
Study Director

Date

2. QUALITY ASSURANCE STATEMENT

BioReliance by SAFC

Quality Assurance Statement

Study Information

Number: AF28PN.503.BTL

Compliance

Procedures, documentation, equipment and other records were examined in order to assure this study was performed in accordance with the regulation(s) listed below and conducted according to the protocol and relevant Standard Operating Procedures. Verification of the study protocol was performed and documented by Quality Assurance.

US EPA Good Laboratory Standards 40CFR 792

Inspections

Quality Assurance performed the inspections(s) below for this study.

Insp. Dates (From/To)		Phase Inspected	To Study Director	To Management
14-Jun-2018	15-Jun-2018	Protocol Review	15-Jun-2018	15-Jun-2018
19-Jun-2018	19-Jun-2018	Dilution of the test article and/or positive control	20-Jun-2018	20-Jun-2018
13-Jul-2018	13-Jul-2018	Data/Draft Report	13-Jul-2018	13-Jul-2018
23-Aug-2018	23-Aug-2018	Final Report	23-Aug-2018	23-Aug-2018
23-Aug-2018	23-Aug-2018	Protocol Amendment Review	23-Aug-2018	23-Aug-2018

The Final Report for this study describes the methods and procedures used in the study and the reported results accurately reflect the raw data of the study.

For a multisite study, test site QA Statements are located in the corresponding contributing scientist report.

E-signature

Quality Assurance: Carlos Bonilla 27-Aug-2018 6:30 pm GMT

Reason for signature: QA Approval

Printed by:Carlos Bonilla

Printed on:27-Aug-18

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4. STUDY INFORMATION

Study Conduct

Sponsor:

Sponsor's Authorized Representative:

Testing Facility:	BioReliance Corporation 9630 Medical Center Drive Rockville, MD 20850
BioReliance Study No.:	AF28PN.503.BTL
Sponsor No.:	

Test Substance

Identification:

Description:	White powder
Storage Conditions:	Room temperature, protected from light
Receipt Date:	02 May 2018

Study Dates

Study Initiation Date:	01 June 2018
Experimental Starting Date (first day of data collection):	01 June 2018
Experimental Start Date (first day test substance administered to test system):	05 June 2018
Experimental Completion Date:	26 June 2018

Key Personnel

Study Director:	Emily Dakoulas, BS

Testing Facility Management:	Rohan Kulkarni, MSc, Ph.D. Director, Genetic Toxicology Study Management
Laboratory Supervisor:	Ankit Patel, BS
Report Writer:	Gayathri Jayakumar, MPS

5. SUMMARY

The test substance, was tested to evaluate its mutagenic potential by measuring its ability to induce reverse mutations at selected loci of several strains of *Salmonella typhimurium* and at the tryptophan locus of *Escherichia coli* strain WP2 *uvr*A in the presence and absence of an exogenous metabolic activation system. Water was used as the vehicle.

In the initial toxicity-mutation assay, the dose levels tested were 1.50, 5.00, 15.0, 50.0, 150, 500, 1500 and 5000 µg per plate. Neither precipitate nor toxicity was observed. No positive mutagenic responses were observed with any of the tester strains in either the presence or absence of S9 activation. Based upon these results, the maximum dose tested in the confirmatory mutagenicity assay was 5000 µg per plate.

In the confirmatory mutagenicity assay, the dose levels tested were 50.0, 150, 500, 1500 and 5000 µg per plate. Neither precipitate nor toxicity was observed. No positive mutagenic responses were observed with any of the tester strains in either the presence or absence of S9 activation.

These results indicate was negative for the ability to induce reverse mutations at selected loci of several strains of *Salmonella typhimurium* and at the tryptophan locus of *Escherichia coli* strain WP2 *uvr*A in the presence and absence of an exogenous metabolic activation system.

6. PURPOSE

The purpose of this study was to evaluate the mutagenic potential of the test substance by measuring its ability to induce reverse mutations at selected loci of several strains of *Salmonella typhimurium* and at the tryptophan locus of *Escherichia coli* strain WP2 *uvr*A in the presence and absence of an exogenous metabolic activation system.

Historical control data are found in Appendix I. Copies of the study protocol and amendment are included in Appendix II.

7. CHARACTERIZATION OF TEST AND CONTROL SUBSTANCES

The identity, strength, purity, stability and composition or other characteristics to define the test substance have not been determined.

All unused Test Substance was returned to the sponsor prior to report finalization using the information below.

The vehicle used to deliver to the test system was water.

Vehicle	CAS Number	Supplier	Lot Number	Purity	Expiration Date
Water	7732-18-5	Sigma-Aldrich	RNBF9658	Sterile-filtered	Mar 2019
			RNBG4913		Dec 2019

To achieve a solution, the most concentrated dilution was sonicated at 21.4ºC for 1 minute in the initial toxicity-mutation assay. Test substance dilutions were prepared immediately before use and delivered to the test system at room temperature under filtered light.

Positive controls plated concurrently with each assay are listed in the following table. All positive controls were diluted in dimethyl sulfoxide (DMSO) except for sodium azide, which was diluted in sterile water. All subdivided solutions of positive controls were stored at -10 to -30°C.

Strain	S9 Activation	Positive Control	Concentration (µg/plate)
TA98, TA1535	Rat	2-aminoanthracene (Sigma Aldrich Chemical Co., Inc.) Lot No. STBD3302V Exp. Date 30-Nov-2019 CAS No. 613-13-8 Purity 97.5%	1.0
TA100, TA1537			2.0
WP2 *uvr*A			15
TA98	None	2-nitrofluorene (Sigma Aldrich Chemical Co., Inc.) Lot No. S43858V Exp. Date 31-Mar-2019 CAS No. 607-57-8 Purity 99.4%	1.0
TA100, TA1535		sodium azide (Sigma Aldrich Chemical Co., Inc.) Lot No. MKBT8080V Exp. Date Jan-2020 CAS No. 26628-22-8 Purity 99.8%	1.0
TA1537		9-aminoacridine (Sigma Aldrich Chemical Co., Inc.) Lot No. BCBK1177V Exp. Date 31-Mar-2019 CAS No. 52417-22-8 Purity 99.5%	75
WP2 *uvr*A		methyl methanesulfonate (Sigma Aldrich Chemical Co., Inc.) Lot No. MKBX5165V Exp. Date 31-Oct-2020 CAS No. 66-27-3 Purity 99.5%	1,000

The negative and positive control substances have been characterized as per the Certificates of Analysis on file with the testing facility. The stability of the negative and positive control substances and their mixtures was demonstrated by acceptable results that met the criteria for a valid test.

Dose Formulation Collection and Analysis

Analyses to determine the concentration, uniformity and stability of the test substance dose formulations were not performed.

8. MATERIALS AND METHODS

Test System

The tester strains used were the *Salmonella typhimurium* histidine auxotrophs TA98, TA100, TA1535 and TA1537 as described by Ames *et al*. (1975) and *Escherichia coli* WP2 *uvr*A as described by Green and Muriel (1976).

Tester strains TA98 and TA1537 are reverted from histidine dependence (auxotrophy) to histidine independence (prototrophy) by frameshift mutagens. Tester strain TA1535 is reverted by mutagens that cause basepair substitutions. Tester strain TA100 is reverted by mutagens that cause both frameshift and basepair substitution mutations. Specificity of the reversion mechanism in *E. coli* is sensitive to basepair substitution mutations, rather than frameshift mutations (Green and Muriel, 1976).

Salmonella tester strains were derived from Dr. Bruce Ames' cultures; *E. coli* tester strains were from the National Collection of Industrial and Marine Bacteria, Aberdeen, Scotland.

Solubility Determination

Water was the vehicle of choice based on the solubility of the test substance and compatibility with the target cells. The test substance formed a clear solution in water at a concentration of approximately 50 mg/mL in the solubility test conducted at BioReliance.

Preparation of Tester Strain

Overnight cultures were prepared by inoculating from the appropriate frozen permanent stock into a vessel, containing 30 to 50 mL of culture medium. To assure that cultures were harvested in late log phase, the length of incubation was controlled and monitored. Following inoculation, each flask was placed in a shaker/incubator programmed to begin shaking at 125 to 175 rpm and incubating at 37±2°C for approximately 12 hours before the anticipated time of harvest. Each culture was monitored spectrophotometrically for turbidity and was harvested at a percent transmittance yielding a titer of greater than or equal to 0.3×10^9 cells per milliliter. The actual titers were determined by viable count assays on nutrient agar plates.

Identification of Test System

Each plate was identified by the BioReliance study number and a code system to designate the treatment condition, dose level and test phase, as described in detail in BioReliance's Standard Operating Procedures.

Metabolic Activation System

Aroclor 1254-induced rat liver S9 was used as the metabolic activation system. The S9 was prepared from male Sprague-Dawley rats that were injected intraperitoneally with Aroclor™ 1254 (200 mg/mL in corn oil) at a dose of 500 mg/kg, five days before sacrifice. The S9 (Lot No. 3925, Exp. Date: 21 Feb 2020; Lot No. 3961, Exp. Date: 15 May 2020) was purchased

commercially from MolTox (Boone, NC). Upon arrival at BioReliance, the S9 was stored at -60°C or colder until used. Each bulk preparation of S9 was assayed for its ability to metabolize benzo(a)pyrene and 2-aminoanthracene to forms mutagenic to *Salmonella typhimurium* TA100.

The S9 mix was prepared on the day of use as indicated below:

Component	Final Concentration
β-nicotinamide-adenine dinucleotide phosphate	4 mM
Glucose-6-phosphate	5 mM
Potassium chloride	33 mM
Magnesium chloride	8 mM
Phosphate Buffer (pH 7.4)	100 mM
S9 homogenate	10% (v/v)

The Sham mixture (Sham mix), containing 100 mM phosphate buffer at pH 7.4, was also prepared on the day of use.

Frequency and Route of Administration

The test system was exposed to the test substance via the plate incorporation methodology originally described by Ames *et al.* (1975) and updated by Maron and Ames (1983).

Initial Toxicity-Mutation Assay to Select Dose Levels

The initial toxicity-mutation assay was used to establish the dose-range for the confirmatory mutagenicity assay and to provide a preliminary mutagenicity evaluation. TA98, TA100, TA1535, TA1537 and WP2 *uvr*A were exposed to the vehicle alone, positive controls and eight dose levels of the test substance, in duplicate, in the presence and absence of Aroclor-induced rat liver S9. Dose levels for the confirmatory mutagenicity assay were based upon lack of post-treatment toxicity.

Confirmatory Mutagenicity Assay

The confirmatory mutagenicity assay was used to evaluate and confirm the mutagenic potential of the test substance. TA98, TA100, TA1535, TA1537 and WP2 *uvr*A were exposed to the vehicle alone, positive controls and five dose levels of the test substance, in triplicate, in the presence and absence of Aroclor-induced rat liver S9.

Treatment of Test System

Media used in the treatment of the test system were as indicated below.

Component	Medium			
	Minimal top agar	Minimal bottom agar	Nutrient bottom agar	Nutrient broth
	Concentration in Medium			
BBL Select agar (W/V)	0.8% (W/V)	--	--	--
Vogel-Bonner minimal medium E	--	1.5% (W/V)	1.5% (W/V)	--
Sodium chloride	0.5% (W/V)	--	--	--
L-histidine, D-biotin and L-tryptophan solution	50 mM each	--	--	--
Sterile water	25 mL/100 mL agar (when agar not used with S9 or Sham mix)	--	--	--
Oxoid Nutrient Broth No. 2 (dry powder)	--	--	2.5% (W/V)	2.5% (W/V)
Vogel-Bonner salt solution	--	--	--	Supplied at 20 mL/L

To confirm the sterility of the S9 and Sham mixes, a 0.5 mL aliquot of each was plated on selective agar. To confirm the sterility of the test substance and the vehicle, all test substance dose levels and the vehicle used in each assay were plated on selective agar with an aliquot volume equal to that used in the assay. These plates were incubated under the same conditions as the assay.

One-half (0.5) milliliter of S9 or Sham mix, 100 µL of tester strain (cells seeded) and 100 µL of vehicle or test substance dilution were added to 2.0 mL of molten selective top agar at 45±2°C. When plating the positive controls, the test substance aliquot was replaced by a 50.0 µL aliquot of appropriate positive control. After vortexing, the mixture was overlaid onto the surface of 25 mL of minimal bottom agar. After the overlay had solidified, the plates were inverted and incubated for 48 to 72 hours at 37±2°C. Plates that were not counted immediately following the incubation period were stored at 2-8°C until colony counting could be conducted.

Scoring

The condition of the bacterial background lawn was evaluated for evidence of test substance toxicity by using a dissecting microscope. Precipitate was evaluated after the incubation period by visual examination without magnification. Toxicity and degree of precipitation were scored relative to the vehicle control plate using the codes shown in the following table. As appropriate, colonies were enumerated either by hand or by machine.

Code	Description	Characteristics
1 or no code	Normal	Distinguished by a healthy microcolony lawn.
2	Slightly Reduced	Distinguished by a noticeable thinning of the microcolony lawn and possibly a slight increase in the size of the microcolonies compared to the vehicle control plate.
3	Moderately Reduced	Distinguished by a marked thinning of the microcolony lawn resulting in a pronounced increase in the size of the microcolonies compared to the vehicle control plate.
4	Extremely Reduced	Distinguished by an extreme thinning of the microcolony lawn resulting in an increase in the size of the microcolonies compared to the vehicle control plate such that the microcolony lawn is visible to the unaided eye as isolated colonies.
5	Absent	Distinguished by a complete lack of any microcolony lawn over greater than or equal to 90% of the plate.
6	Obscured by Particulate	The background bacterial lawn cannot be accurately evaluated due to microscopic test substance particulate.
NP	Non-Interfering Precipitate	Distinguished by precipitate on the plate that is visible to the naked eye but any precipitate particles detected by the automated colony counter total less than or equal to 10% of the revertant colony count (e.g., less than or equal to 3 particles on a plate with 30 revertants).
IP	Interfering Precipitate	Distinguished by precipitate on the plate that is visible to the naked eye and any precipitate particles detected by the automated colony counter exceed 10% of the revertant colony count (e.g., greater than 3 particles on a plate with 30 revertants). These plates are counted manually.

Tester Strain Verification

On the day of use in each assay, all tester strain cultures were checked for the appropriate genetic markers.

Criteria for a Valid Test

The following criteria must be met for each assay to be considered valid:

All *Salmonella* tester strain cultures must demonstrate the presence of the deep rough mutation (*rfa*) and the deletion in the *uvr*B gene. Cultures of tester strains TA98 and TA100 must demonstrate the presence of the pKM101 plasmid R-factor. All WP2 *uvr*A cultures must demonstrate the deletion in the *uvr*A gene.

Based on historical control data (95% control limits), all tester strain cultures must exhibit characteristic numbers of spontaneous revertants per plate with the vehicle controls. The mean revertants per plate must be within the following ranges (inclusive).

95% Control Limits (99% Upper Limit)					
	TA98	TA100	TA1535	TA1537	WP2 *uvr*A
-S9	5-25 (30)	66-114 (126)	4-20 (24)	2-14 (17)	10-38 (45)
+S9	10-34 (40)	66-122 (136)	4-20 (24)	3-15 (18)	13-41 (48)
With Study Director justification, values including the 99% control limit and above are acceptable.					

To ensure that appropriate numbers of bacteria are plated, tester strain culture titers must be greater than or equal to $0.3x10^9$ cells/mL.

The mean of each positive control must exhibit at least a 3.0-fold increase in the number of revertants over the mean value of the respective vehicle control and exceed the corresponding acceptable vehicle control range cited above.

A minimum of three non-toxic dose levels is required to evaluate assay data. A dose level is considered toxic if one or both of the following criteria are met: (1) A >50 % reduction in the mean number of revertants per plate as compared to the mean vehicle control value. This reduction must be accompanied by an abrupt dose-dependent drop in the revertant count. (2) At least a moderate reduction in the background lawn (background code 3, 4 or 5).

Evaluation of Test Results

For each replicate plating, the mean and standard deviation of the number of revertants per plate were calculated and are reported.

For the test substance to be evaluated positive, it must cause a dose-related increase in the mean revertants per plate of at least one tester strain over a minimum of two increasing concentrations of test substance as specified below:

Strains TA1535 and TA1537

Data sets were judged positive if the increase in mean revertants at the peak of the dose response was equal to or greater than 3.0-times the mean vehicle control value and above the corresponding acceptable vehicle control range.

Strains TA98, TA100 and WP2 *uvr*A

Data sets were judged positive if the increase in mean revertants at the peak of the dose response was equal to or greater than 2.0-times the mean vehicle control value and above the corresponding acceptable vehicle control range.

An equivocal response is a biologically relevant increase in a revertant count that partially meets the criteria for evaluation as positive. This could be a dose-responsive increase that does not achieve the respective threshold cited above or a non-dose responsive increase that is equal to or greater than the respective threshold cited. A response was evaluated as negative if it was neither positive nor equivocal.

Electronic Data Collection Systems

The primary computer or electronic systems used for the collection of data or analysis included but were not limited to the following:

System	Purpose
LIMS Labware System	Test Substance Tracking
Excel 2007 (Microsoft Corporation)	Calculations
Sorcerer Colony Counter and Ames Study Manager (Perceptive Instruments)	Data Collection/Table Creation
Kaye Lab Watch Monitoring system (Kaye GE)	Environmental Monitoring
BRIQS	Deviation and audit reporting

Records and Archives

All raw data, the original signed protocol, amendment(s) (if applicable), and the original signed final report will be archived by BioReliance at JK Records as directed by the applicable SOP. A copy of the draft report, including Study Director and Sponsor comments, if applicable, will be archived electronically by BioReliance. Following the SOP retention period, the Sponsor will be contacted by BioReliance for disposition instructions or return of materials. Slides and/or specimens (as applicable) will be archived at EPL Archives and indexed as such in the BioReliance archive database.

BioReliance reserves the right to retain true copies (i.e. photocopies, scans, microfilm, or other accurate reproductions of the original records) for at least the minimum retention period specified by the relevant regulations.

Deviations

No deviations from the protocol or assay-method SOPs occurred during the conduct of this study.

9. RESULTS AND DISCUSSION

Sterility Results

No contaminant colonies were observed on the sterility plates for the vehicle control, the test substance dilutions or the S9 and Sham mixes.

Tester Strain Titer Results

Experiment	Tester Strain				
	TA98	TA100	TA1535	TA1537	WP2 *uvr*A
	Titer Value (x 10^9 cells per mL)				
B1	2.2	1.0	0.8	1.5	2.9
B2	1.2	1.1	1.5	1.9	2.8

Initial Toxicity-Mutation Assay

The results of the initial toxicity-mutation assay conducted at dose levels of 1.50, 5.00, 15.0, 50.0, 150, 500, 1500 and 5000 µg per plate in water are presented in Tables 1 and 2. The maximum dose of 5000 µg per plate was achieved using a concentration of 50.0 mg/mL and a 100 µL plating aliquot.

Neither precipitate nor toxicity was observed.

No positive mutagenic responses were observed with any of the tester strains in either the presence or absence of S9 activation.

Confirmatory Mutagenicity Assay

The results of the confirmatory mutagenicity assay are presented in Tables 3 and 4. Based upon the results of the initial toxicity-mutation assay, the dose levels selected for the confirmatory mutagenicity assay were 50.0, 150, 500, 1500 and 5000 µg per plate.

Neither precipitate nor toxicity was observed. No positive mutagenic responses were observed with any of the tester strains in either the presence or absence of S9 activation.

A copy of the Common Technical Document Tables is included in Appendix III.

10. CONCLUSION

All criteria for a valid study were met as described in the protocol. The results of the Bacterial Reverse Mutation Assay indicate that, under the conditions of this study, did not cause a positive mutagenic response with any of the tester strains in either the presence or absence of Aroclor-induced rat liver S9.

11. REFERENCES

Ames, B.N., J. McCann and E. Yamasaki (1975) Methods for Detecting Carcinogens and Mutagens with the *Salmonella*/Mammalian Microsome Mutagenicity Test, Mutation Research, 31:347-364.

Green, M.H.L. and W.J. Muriel (1976) Mutagen testing using trp+ reversion in *Escherichia coli*, Mutation Research 38:3-32.

ISO/IEC 17025:2005, General requirements for the competence of testing and calibration laboratories.

Maron, D.M. and B.N. Ames (1983) Revised Methods for the *Salmonella* Mutagenicity Test, Mutation Research, 113:173-215.

OECD Guideline 471 (Genetic Toxicology: Bacterial Reverse Mutation Test), Ninth Addendum to the OECD Guidelines for the Testing of Chemicals, adopted July 21, 1997.

12. DATA TABLES

TABLE 1
Initial Toxicity-Mutation Assay without S9 activation

Study Number: AF28PN.503.BTL
Experiment: B1
Exposure Method: Plate incorporation assay
Study Code: AF28PN
Date Plated: 6/5/2018
Evaluation Period: 6/11/2018

Strain	Substance	Dose level per plate	Mean revertants per plate	Standard Deviation	Ratio treated / solvent	Individual revertant colony counts and background codes
TA98		5000 µg	*11*	*4*	*0.8*	8[A], 14[A]
		1500 µg	*19*	*6*	*1.4*	15[A], 23[A]
		500 µg	*14*	*1*	*1.0*	15[A], 13[A]
		150 µg	*11*	*5*	*0.8*	7[A], 14[A]
		50.0 µg	*14*	*6*	*1.0*	10[A], 18[A]
		15.0 µg	*12*	*3*	*0.9*	10[A], 14[A]
		5.00 µg	*9*	*0*	*0.6*	9[A], 9[A]
		1.50 µg	*10*	*1*	*0.7*	9[A], 10[A]
	Water	100 µL	*14*	*4*		16[A], 11[A]
TA100		5000 µg	*90*	*8*	*1.1*	84[A], 95[A]
		1500 µg	*78*	*3*	*1.0*	80[A], 76[A]
		500 µg	*79*	*4*	*1.0*	76[A], 81[A]
		150 µg	*88*	*1*	*1.1*	87[A], 89[A]
		50.0 µg	*88*	*11*	*1.1*	96[A], 80[A]
		15.0 µg	*75*	*11*	*0.9*	67[A], 83[A]
		5.00 µg	*85*	*2*	*1.1*	83[A], 86[A]
		1.50 µg	*80*	*21*	*1.0*	95[A], 65[A]
	Water	100 µL	*79*	*11*		71[A], 86[A]
TA1535		5000 µg	*10*	*6*	*0.8*	6[A], 14[A]
		1500 µg	*10*	*0*	*0.8*	10[A], 10[A]
		500 µg	*13*	*0*	*1.0*	13[A], 13[A]
		150 µg	*9*	*1*	*0.7*	8[A], 10[A]
		50.0 µg	*13*	*2*	*1.0*	14[A], 11[A]
		15.0 µg	*12*	*1*	*0.9*	13[A], 11[A]
		5.00 µg	*7*	*0*	*0.5*	7[A], 7[A]
		1.50 µg	*11*	*8*	*0.8*	16[A], 5[A]
	Water	100 µL	*13*	*2*		11[A], 14[A]

Key to Automatic Count Flags

[A]: Automatic count

TABLE 1 (CONT.)
Initial Toxicity-Mutation Assay without S9 activation

Study Number: AF28PN.503.BTL
Experiment: B1
Exposure Method: Plate incorporation assay

Study Code: AF28PN
Date Plated: 6/5/2018
Evaluation Period: 6/11/2018

Strain	Substance	Dose level per plate	Mean revertants per plate	Standard Deviation	Ratio treated / solvent	Individual revertant colony counts and background codes
TA1537		5000 µg	*6*	*0*	*1.0*	6[A], 6[A]
		1500 µg	*5*	*3*	*0.8*	7[A], 3[A]
		500 µg	*7*	*0*	*1.2*	7[A], 7[A]
		150 µg	*5*	*2*	*0.8*	3[A], 6[A]
		50.0 µg	*6*	*1*	*1.0*	6[A], 5[A]
		15.0 µg	*7*	*1*	*1.2*	6[A], 8[A]
		5.00 µg	*7*	*0*	*1.2*	7[A], 7[A]
		1.50 µg	*7*	*1*	*1.2*	6[A], 7[A]
	Water	100 µL	*6*	*4*		3[A], 9[A]
WP2uvrA		5000 µg	*35*	*0*	*1.0*	35[A], 35[A]
		1500 µg	*36*	*6*	*1.1*	31[A], 40[A]
		500 µg	*31*	*5*	*0.9*	34[A], 27[A]
		150 µg	*34*	*7*	*1.0*	39[A], 29[A]
		50.0 µg	*30*	*4*	*0.9*	32[A], 27[A]
		15.0 µg	*38*	*12*	*1.1*	46[A], 29[A]
		5.00 µg	*35*	*13*	*1.0*	26[A], 44[A]
		1.50 µg	*36*	*15*	*1.1*	25[A], 46[A]
	Water	100 µL	*34*	*1*		33[A], 34[A]
TA98	**2NF**	1.00 µg	*69*	*21*	*4.9*	83[A], 54[A]
TA100	**SA**	1.00 µg	*600*	*35*	*7.6*	575[A], 625[A]
TA1535	**SA**	1.00 µg	*564*	*21*	*43.4*	549[A], 579[A]
TA1537	**9AAD**	75.0 µg	*858*	*120*	*143.0*	773[A], 943[A]
WP2uvrA	**MMS**	1000 µg	*513*	*25*	*15.1*	531[A], 495[A]

Key to Positive Controls

2NF	2-nitrofluorene
SA	sodium azide
9AAD	9-Aminoacridine
MMS	methyl methanesulfonate

Key to Automatic Count Flags

[A]: Automatic count

TABLE 2
Initial Toxicity-Mutation Assay with S9 activation

Study Number: AF28PN.503.BTL
Experiment: B1
Exposure Method: Plate incorporation assay

Study Code: AF28PN
Date Plated: 6/5/2018
Evaluation Period: 6/11/2018

Strain	Substance	Dose level per plate	Mean revertants per plate	Standard Deviation	Ratio treated / solvent	Individual revertant colony counts and background codes
TA98		5000 µg	*16*	*1*	*0.8*	15[A], 17[A]
		1500 µg	*29*	*4*	*1.4*	26[A], 32[A]
		500 µg	*23*	*1*	*1.1*	22[A], 24[A]
		150 µg	*16*	*3*	*0.8*	18[A], 14[A]
		50.0 µg	*17*	*0*	*0.8*	17[A], 17[A]
		15.0 µg	*22*	*5*	*1.0*	25[A], 18[A]
		5.00 µg	*17*	*8*	*0.8*	22[A], 11[A]
		1.50 µg	*18*	*2*	*0.9*	19[A], 16[A]
	Water	100 µL	*21*	*8*		15[A], 26[A]
TA100		5000 µg	*108*	*7*	*1.1*	103[A], 113[A]
		1500 µg	*104*	*15*	*1.0*	93[A], 114[A]
		500 µg	*98*	*1*	*1.0*	97[A], 99[A]
		150 µg	*125*	*23*	*1.2*	108[A], 141[A]
		50.0 µg	*106*	*1*	*1.0*	107[A], 105[A]
		15.0 µg	*101*	*4*	*1.0*	103[A], 98[A]
		5.00 µg	*102*	*6*	*1.0*	106[A], 98[A]
		1.50 µg	*98*	*4*	*1.0*	100[A], 95[A]
	Water	100 µL	*101*	*7*		106[A], 96[A]
TA1535		5000 µg	*18*	*6*	*1.3*	13[A], 22[A]
		1500 µg	*12*	*2*	*0.9*	13[A], 10[A]
		500 µg	*12*	*3*	*0.9*	10[A], 14[A]
		150 µg	*13*	*6*	*0.9*	9[A], 17[A]
		50.0 µg	*13*	*4*	*0.9*	16[A], 10[A]
		15.0 µg	*12*	*4*	*0.9*	9[A], 14[A]
		5.00 µg	*11*	*4*	*0.8*	8[A], 13[A]
		1.50 µg	*7*	*1*	*0.5*	6[A], 8[A]
	Water	100 µL	*14*	*5*		10[A], 17[A]

Key to Automatic Count Flags

[A]: Automatic count

TABLE 2 (CONT.)
Initial Toxicity-Mutation Assay with S9 activation

Study Number: AF28PN.503.BTL
Experiment: B1
Exposure Method: Plate incorporation assay

Study Code: AF28PN
Date Plated: 6/5/2018
Evaluation Period: 6/11/2018

Strain	Substance	Dose level per plate	Mean revertants per plate	Standard Deviation	Ratio treated / solvent	Individual revertant colony counts and background codes
TA1537		5000 µg	*5*	*2*	*0.8*	6[A], 3[A]
		1500 µg	*8*	*1*	*1.3*	9[A], 7[A]
		500 µg	*4*	*3*	*0.7*	2[A], 6[A]
		150 µg	*7*	*2*	*1.2*	5[A], 8[A]
		50.0 µg	*4*	*2*	*0.7*	5[A], 2[A]
		15.0 µg	*4*	*1*	*0.7*	5[A], 3[A]
		5.00 µg	*6*	*1*	*1.0*	6[A], 5[A]
		1.50 µg	*5*	*2*	*0.8*	6[A], 3[A]
	Water	100 µL	*6*	*1*		6[A], 5[A]
WP2uvrA		5000 µg	*35*	*1*	*1.2*	34[A], 36[A]
		1500 µg	*37*	*8*	*1.2*	31[A], 42[A]
		500 µg	*32*	*1*	*1.1*	32[A], 31[A]
		150 µg	*30*	*1*	*1.0*	29[A], 31[A]
		50.0 µg	*29*	*4*	*1.0*	31[A], 26[A]
		15.0 µg	*29*	*6*	*1.0*	33[A], 24[A]
		5.00 µg	*31*	*1*	*1.0*	31[A], 30[A]
		1.50 µg	*33*	*11*	*1.1*	25[A], 41[A]
	Water	100 µL	*30*	*4*		27[A], 32[A]
TA98	**2AA**	1.00 µg	*239*	*19*	*11.4*	225[A], 252[A]
TA100	**2AA**	2.00 µg	*547*	*7*	*5.4*	552[A], 542[A]
TA1535	**2AA**	1.00 µg	*83*	*6*	*5.9*	87[A], 79[A]
TA1537	**2AA**	2.00 µg	*70*	*26*	*11.7*	88[A], 51[A]
WP2uvrA	**2AA**	15.0 µg	*247*	*16*	*8.2*	235[A], 258[A]

Key to Positive Controls

2AA 2-aminoanthracene

Key to Automatic Count Flags

[A]: Automatic count

TABLE 3
Confirmatory Mutagenicity Assay without S9 activation

Study Number: AF28PN.503.BTL
Experiment: B2
Exposure Method: Plate incorporation assay
Study Code: AF28PN
Date Plated: 6/19/2018
Evaluation Period: 6/26/2018

Strain	Substance	Dose level per plate	Mean revertants per plate	Standard Deviation	Ratio treated / solvent	Individual revertant colony counts and background codes
TA98		5000 µg	*13*	*3*	*1.0*	16^{A}, 13^{A}, 11^{A}
		1500 µg	*13*	*5*	*1.0*	18^{A}, 8^{A}, 13^{A}
		500 µg	*11*	*3*	*0.8*	8^{A}, 13^{A}, 13^{A}
		150 µg	*13*	*3*	*1.0*	11^{A}, 16^{A}, 13^{A}
		50.0 µg	*13*	*4*	*1.0*	10^{A}, 17^{A}, 13^{A}
	Water	100 µL	*13*	*2*		14^{A}, 14^{A}, 11^{A}
TA100		5000 µg	*73*	*22*	*0.9*	68^{A}, 55^{A}, 97^{A}
		1500 µg	*89*	*9*	*1.2*	89^{A}, 81^{A}, 98^{A}
		500 µg	*92*	*6*	*1.2*	92^{A}, 86^{A}, 98^{A}
		150 µg	*83*	*3*	*1.1*	80^{A}, 82^{A}, 86^{A}
		50.0 µg	*83*	*8*	*1.1*	76^{A}, 83^{A}, 91^{A}
	Water	100 µL	*77*	*9*		87^{A}, 72^{A}, 71^{A}
TA1535		5000 µg	*12*	*4*	*1.0*	8^{A}, 15^{A}, 14^{A}
		1500 µg	*10*	*4*	*0.8*	13^{A}, 11^{A}, 6^{A}
		500 µg	*9*	*2*	*0.8*	9^{A}, 11^{A}, 7^{A}
		150 µg	*16*	*1*	*1.3*	16^{A}, 17^{A}, 16^{A}
		50.0 µg	*10*	*5*	*0.8*	6^{A}, 15^{A}, 10^{A}
	Water	100 µL	*12*	*3*		13^{A}, 9^{A}, 14^{A}
TA1537		5000 µg	*4*	*2*	*0.8*	3^{A}, 3^{A}, 6^{A}
		1500 µg	*5*	*0*	*1.0*	5^{A}, 5^{A}, 5^{A}
		500 µg	*7*	*2*	*1.4*	7^{A}, 5^{A}, 9^{A}
		150 µg	*7*	*4*	*1.4*	11^{A}, 3^{A}, 6^{A}
		50.0 µg	*6*	*3*	*1.2*	6^{A}, 3^{A}, 9^{A}
	Water	100 µL	*5*	*2*		3^{A}, 6^{A}, 6^{A}

Key to Automatic Count Flags

^{A}: Automatic count

TABLE 3 (CONT.)
Confirmatory Mutagenicity Assay without S9 activation

Study Number: AF28PN.503.BTL
Experiment: B2
Exposure Method: Plate incorporation assay
Study Code: AF28PN
Date Plated: 6/19/2018
Evaluation Period: 6/26/2018

Strain	Substance	Dose level per plate	Mean revertants per plate	Standard Deviation	Ratio treated / solvent	Individual revertant colony counts and background codes
WP2uvrA		5000 µg	*35*	*1*	*1.1*	36[A], 35[A], 35[A]
		1500 µg	*37*	*4*	*1.1*	42[A], 34[A], 36[A]
		500 µg	*34*	*6*	*1.0*	31[A], 41[A], 31[A]
		150 µg	*40*	*9*	*1.2*	41[A], 48[A], 31[A]
		50.0 µg	*24*	*9*	*0.7*	15[A], 24[A], 32[A]
	Water	100 µL	*33*	*3*		35[A], 30[A], 34[A]
TA98	**2NF**	1.00 µg	*52*	*14*	*4.0*	40[A], 48[A], 67[A]
TA100	**SA**	1.00 µg	*653*	*24*	*8.5*	627[A], 657[A], 675[A]
TA1535	**SA**	1.00 µg	*590*	*30*	*49.2*	611[A], 603[A], 556[A]
TA1537	**9AAD**	75.0 µg	*521*	*129*	*104.2*	388[A], 529[A], 645[A]
WP2uvrA	**MMS**	1000 µg	*462*	*38*	*14.0*	487[A], 418[A], 480[A]

Key to Positive Controls

2NF	2-nitrofluorene
SA	sodium azide
9AAD	9-Aminoacridine
MMS	methyl methanesulfonate

Key to Automatic Count Flags

[A]: Automatic count

TABLE 4
Confirmatory Mutagenicity Assay with S9 activation

Study Number: AF28PN.503.BTL
Experiment: B2
Exposure Method: Plate incorporation assay
Study Code: AF28PN
Date Plated: 6/19/2018
Evaluation Period: 6/26/2018

Strain	Substance	Dose level per plate	Mean revertants per plate	Standard Deviation	Ratio treated / solvent	Individual revertant colony counts and background codes
TA98		5000 µg	*14*	*1*	*1.0*	15[A], 14[A], 14[A]
		1500 µg	*15*	*2*	*1.1*	17[A], 13[A], 14[A]
		500 µg	*14*	*4*	*1.0*	17[A], 15[A], 9[A]
		150 µg	*17*	*4*	*1.2*	16[A], 22[A], 14[A]
		50.0 µg	*17*	*5*	*1.2*	22[A], 13[A], 17[A]
	Water	100 µL	*14*	*2*		16[A], 13[A], 14[A]
TA100		5000 µg	*94*	*5*	*0.9*	88[A], 98[A], 96[A]
		1500 µg	*92*	*10*	*0.9*	98[A], 81[A], 97[A]
		500 µg	*94*	*10*	*0.9*	98[A], 101[A], 83[A]
		150 µg	*101*	*4*	*1.0*	105[A], 98[A], 101[A]
		50.0 µg	*89*	*2*	*0.9*	91[A], 88[A], 87[A]
	Water	100 µL	*100*	*7*		96[A], 108[A], 97[A]
TA1535		5000 µg	*13*	*5*	*1.3*	18[A], 10[A], 10[A]
		1500 µg	*12*	*1*	*1.2*	11[A], 13[A], 11[A]
		500 µg	*8*	*2*	*0.8*	9[A], 9[A], 5[A]
		150 µg	*10*	*4*	*1.0*	8[A], 14[A], 7[A]
		50.0 µg	*8*	*2*	*0.8*	8[A], 7[A], 10[A]
	Water	100 µL	*10*	*2*		11[A], 11[A], 8[A]
TA1537		5000 µg	*8*	*3*	*1.3*	11[A], 6[A], 7[A]
		1500 µg	*5*	*2*	*0.8*	6[A], 2[A], 6[A]
		500 µg	*6*	*1*	*1.0*	7[A], 5[A], 5[A]
		150 µg	*5*	*3*	*0.8*	9[A], 3[A], 3[A]
		50.0 µg	*7*	*2*	*1.2*	5[A], 6[A], 9[A]
	Water	100 µL	*6*	*1*		5[A], 7[A], 5[A]

Key to Automatic Count Flags

[A]: Automatic count

TABLE 4 (CONT.)
Confirmatory Mutagenicity Assay with S9 activation

Study Number: AF28PN.503.BTL
Experiment: B2
Exposure Method: Plate incorporation assay

Study Code: AF28PN
Date Plated: 6/19/2018
Evaluation Period: 6/26/2018

Strain	Substance	Dose level per plate	Mean revertants per plate	Standard Deviation	Ratio treated / solvent	Individual revertant colony counts and background codes
WP2uvrA		5000 µg	*31*	*2*	*1.1*	30^{A}, 30^{A}, 34^{A}
		1500 µg	*31*	*3*	*1.1*	33^{A}, 33^{A}, 27^{A}
		500 µg	*34*	*6*	*1.2*	39^{A}, 36^{A}, 27^{A}
		150 µg	*36*	*9*	*1.2*	46^{A}, 31^{A}, 30^{A}
		50.0 µg	*31*	*3*	*1.1*	29^{A}, 30^{A}, 35^{A}
	Water	100 µL	*29*	*5*		32^{A}, 23^{A}, 32^{A}
TA98	**2AA**	1.00 µg	*217*	*15*	*15.5*	218^{A}, 231^{A}, 202^{A}
TA100	**2AA**	2.00 µg	*778*	*19*	*7.8*	772^{A}, 763^{A}, 800^{A}
TA1535	**2AA**	1.00 µg	*74*	*16*	*7.4*	60^{A}, 91^{A}, 72^{A}
TA1537	**2AA**	2.00 µg	*40*	*6*	*6.7*	35^{A}, 47^{A}, 38^{A}
WP2uvrA	**2AA**	15.0 µg	*289*	*1*	*10.0*	290^{A}, 290^{A}, 288^{A}

Key to Positive Controls

2AA 2-aminoanthracene

Key to Automatic & Manual Count Flags

^{M}: Manual count ^{A}: Automatic count

13. APPENDIX I: Historical Control Data

Historical Negative and Positive Control Values
2016
revertants per plate

Strain	Control	Activation									
		None					Rat Liver				
		Mean	SD	Min	Max	95% CL	Mean	SD	Min	Max	95% CL
TA98	Neg	15	5	6	34	5-25	22	6	8	42	10-34
	Pos	198	174	36	1826		287	159	47	1916	
TA100	Neg	90	12	60	146	66-114	94	14	63	181	66-122
	Pos	629	159	186	1383		620	294	192	3483	
TA1535	Neg	12	4	3	31	4-20	12	4	3	26	4-20
	Pos	541	164	34	1082		150	122	27	1114	
TA1537	Neg	8	3	1	21	2-14	9	3	2	23	3-15
	Pos	368	227	21	1791		91	90	17	951	
WP2 *uvr*A	Neg	24	7	7	44	10-38	27	7	8	51	13-41
	Pos	336	119	25	876		300	111	41	1059	

SD=standard deviation; Min=minimum value; Max=maximum value; 95% CL = Mean ±2 SD (but not less than zero); Neg=negative control (including but not limited to deionized water, dimethyl sulfoxide, ethanol and acetone); Pos=positive control

14. APPENDIX II: Study Protocol and Amendment

PROTOCOL AMENDMENT 1

BioReliance Study No.: AF28PN.503.BTL; **Sponsor No.:**

Title: Bacterial Reverse Mutation Assay

1. Page 7, Section 8, Experimental Design and Methodology – Confirmatory Mutagenicity Assay

   Effective: Date of Study Director signature on this amendment

   Add:
   The doses will be 5000, 1500, 500, 150 and 50.0 µg per plate.

   Reason: To specify the dose levels to be used for the confirmatory assay based on the toxicity and precipitate profiles observed in the initial toxicity-mutation assay.

PROTOCOL AMENDMENT 1

BioReliance Study No.: AF28PN.503.BTL; **Sponsor No.:**

Title: Bacterial Reverse Mutation Assay

Sponsor Approval:

PROTOCOL AMENDMENT 1

BioReliance Study No.: AF28PN.503.BTL; **Sponsor No.:**

Title: Bacterial Reverse Mutation Assay

Study Director and Test Facility Management Approvals:

Emily Dakoulas, BS
BioReliance Study Director

18 Jun 2018
Date

BioReliance Study Management

18 Jun 2018
Date

BioReliance
by SAFC

Protocol

Study Title	**Bacterial Reverse Mutation Assay**
Study Director	Emily Dakoulas, BS
Testing Facility	BioReliance Corporation 9630 Medical Center Drive Rockville, MD 20850
BioReliance Study Number	AF28PN.503.BTL

1. KEY PERSONNEL

Sponsor Information:

Sponsor	
Sponsor Number	
Sponsor's Authorized Representative	

Test Facility Information:

Study Director	Emily Dakoulas, BS BioReliance Corporation Phone: 301-610-2153 Email: emily.dakoulas@sial.com
BioReliance Quality Assurance Representative	Luleayenwa (Lula) Aberra-Degu, RQAP-GLP BioReliance Corporation Phone: 301-610-2667 Email: Luleayenwa.aberra-degu@sial.com

2. TEST SCHEDULE

Proposed Experimental Initiation Date	06-June-2018
Proposed Experimental Completion Date	03-July-2018
Proposed Report Date	18-July-2018

3. REGULATORY REQUIREMENTS

This study will be performed in compliance with the following Good Laboratory Practices (GLP) regulations.

- US EPA GLP Standards 40 CFR 792 (TSCA)

The regulation listed is compatible to non-US regulations, OECD Principles of Good Laboratory Practice (C(97)186/Final); Japanese Ministry of Health, Labor and Welfare Good Laboratory Practices (Ordinance Nos. 21 and 114, if applicable); Japanese Ministry of Agriculture, Forestry and Fisheries Good Laboratory Practices (No. 11 Nousan-6283); Japanese Ministry of Economy, Trade and Industry Good Laboratory Practices, and allows submission of the report under the Mutual Acceptance of Data (MAD) agreement with applicable OECD member countries.

At a minimum, all work performed at US test site(s) will comply with the US GLP regulations stated above. Non-US sites must follow the GLP regulations governing their site. The regulations that were followed will be indicated on the compliance statement in the final contributing report. If no regulatory compliance statement to any GLP regulations is made by the Test Site(s), a GLP exception will be added to the compliance page of the final report.

4. QUALITY ASSURANCE

The protocol, any amendments, at least one in-lab phase, the raw data, draft report(s), and final report(s) will be audited by BioReliance Quality Assurance (QA) and a signed QA Statement will be included in the final report.

Test Site Quality Assurance (where applicable)

At a minimum, Test Site QA is responsible for auditing the raw data and final report(s), and providing the inspection results to the Principal Investigator, Study Director, and their respective management. Additional audits are conducted as directed by Test Site QA SOPS. Email Testing Facility Management at RCK-Tox-TFM@bioreliance.com. A signed QA Statement documenting the type of audits performed, the dates performed, and the dates in which the audit results were reported to the Study Director, Principal Investigator and their respective management must be submitted by the Test Site QA.

5. PURPOSE

The purpose of this study is to evaluate the mutagenic potential of the test substance by measuring its ability to induce reverse mutations at selected loci of several strains of *Salmonella typhimurium* and at the tryptophan locus of *Escherichia coli* WP2 *uvrA* in the presence and absence of an exogenous metabolic activation system. The assay design is based on the OECD Guideline 471, updated and adopted 21 July 1997 and ISO/IEC 17025:2005 (ISO/IEC, 2005).

Storage Conditions	Room Temperature Protect from light (Per BioReliance SOP)
Purity	99.9% (no correction factor will be used for dose formulations)

Characterization of Test Substance
Characterization of the Test Substance is the responsibility of the Sponsor.

Test Substance Reserve Sample
A reserve sample of the Test Substance is the responsibility of the Sponsor.

Characterization of Dose Formulations
Dose formulations will not be analyzed.

Stability of Test Substance in Vehicle
Stability of Test Substance in Vehicle, under the conditions of use, is the responsibility of the Sponsor.

Disposition of Test Substance and Dose Formulations
All unused Test Substance will be returned to the sponsor prior to report finalization using the information below; unless the test substance is used on another study.

Residual dose formulations will be discarded after use.

7. **TEST SYSTEM**
The tester strains will include the *S. typhimurium* histidine auxotrophs TA98, TA100, TA1535 and TA1537 as described by Ames *et al.* (1975) and the *E. coli* tester strain WP2 *uvr*A as described by Green and Muriel (1976). The genotypes of strains are as follows:

Histidine Mutation			Tryptophan Mutation	Additional Mutations		
*his*G46	*his*C3076	*his*D3052	*trp*E	LPS	Repair	R-factor
TA1535	TA1537	-	-	*rfa*	Δ*uvr*B	-
TA100	-	TA98	-	*rfa*	Δ*uvr*B	+R
-	-	-	WP2 *uvr*A	-	Δ*uvr*A	-

The *S. typhimurium* tester strains were from Dr. Bruce Ames, University of California, Berkeley. The *E. coli* tester strain was from the National Collection of Industrial and Marine Bacteria, Aberdeen, Scotland (United Kingdom). The tester strains may also be obtained from Molecular Toxicology Inc. (Moltox).

8. EXPERIMENTAL DESIGN AND METHODOLOGY

The test system will be exposed to the test substance via the plate incorporation methodology originally described by Ames *et al.* (1975) and updated by Maron and Ames (1983). This test system has been shown to detect a wide range of classes of chemical mutagens (McCann *et al.*, 1975; McCann and Ames, 1976).

If the Sponsor is aware of specific metabolic requirements (e.g., azo compounds), this information will be utilized in designing the assay.

Solubility Determination

As needed, a solubility determination will be conducted to determine the maximum soluble concentration or workable suspension as indicated below. Vehicles compatible with this test system, in order of preference, include but are not limited to deionized water (CAS 7732-18-5), dimethyl sulfoxide (CAS 67-68-5), ethanol (CAS 64-17-5) and acetone (CAS 67-64-1). The vehicle of choice, selected in order of preference, will be that which permits preparation of the highest workable or soluble stock concentration, up to 50 mg/ml, for aqueous vehicles and up to 500 mg/mL for organic vehicles. Based on the molecular weight of the test substance, the vehicles to be tested and the dose to be achieved in the assay, alternate stock concentrations may be tested, as needed.

Preparation of Tester Strain

Each tester strain culture will be inoculated from the appropriate frozen stock, lyophilized pellet(s), or master plate. To ensure that cultures are harvested in late log phase, the length of incubation will be controlled and monitored. Each inoculated flask will be placed in a shaker/incubator programmed to begin shaking at 125 to 175 rpm and incubating at 37±2°C.

All cultures will be harvested by spectrophotometric monitoring of culture turbidity rather than by duration of incubation since overgrowth of cultures can cause loss of sensitivity to some mutagens. Cultures will be removed from incubation at a density of approximately 10^9 cells/mL.

Identification of Test System

Each plate will be identified by the BioReliance study number and a code system to designate at least the treatment condition, dose level, and test phase.

Exogenous Metabolic Activation

Liver Homogenate

Liver homogenate (S9) will be purchased commercially (MolTox; Boone, NC). It is prepared from male Sprague-Dawley rats that have been injected intraperitonealy with Aroclor™ 1254 (200 mg/mL in corn oil), at a dose of 500 mg/kg, 5 days before sacrifice.

Sham Mix

100 mM phosphate buffer at pH 7.4

S9 Mix
S9 mix will be prepared on the day of use as indicated below:

Component	Final Concentration
β-nicotinamide-adenine dinucleotide phosphate	4 mM
Glucose-6-phosphate	5 mM
Potassium chloride	33 mM
Magnesium chloride	8 mM
Phosphate Buffer (pH 7.4)	100 mM
S9 homogenate	10% (v/v)

Controls
No analyses will be performed on the positive control articles or the positive control dose formulations. The neat positive control articles and the vehicles used to prepare the test substance and positive control formulations will be characterized by the Certificates of Analysis provided by the Supplier(s). Copies of the Certificates of Analysis will be kept on file at BioReliance.

Vehicle Control
The vehicle for the test substance will be used as the vehicle control for each treatment group. For vehicles with no historical control data, an untreated control will be included.

Sterility Controls
At a minimum, the most concentrated test substance dilution and the Sham and S9 mixes will be checked for sterility.

Positive Controls
Results obtained from these articles will be used to assure responsiveness of the test system but not to provide a standard for comparison with the test substance.

Strain	Positive Control	S9	Concentrations (µg/plate)
Salmonella strains	2-aminoanthracene[B]	+	1.0 – 2.0
WP2 *uvr*A	2-aminoanthracene[B]	+	10 – 20
TA98	2-nitrofluorene[B]	–	1.0
TA100, TA1535	sodium azide[A]	–	1.0
TA1537	9-aminoacridine[B]	–	75
WP2 *uvr*A	methyl methanesulfonate[B]	–	1,000

[A]Prepared in water
[B]Prepared in DMSO

Frequency and Route of Administration
The test system will be treated using the plate incorporation method.

Verification of a clear positive response will not be required (OECD Guideline 471). Equivocal results will be retested in consultation with the Sponsor using an appropriate modification of the experimental design (e.g., dose levels, activation system or treatment method).

Initial Toxicity-Mutation Assay to Select Dose Levels

TA98, TA100, TA1535, TA1537 and WP2 *uvr*A will be exposed to vehicle alone and at least eight concentrations of test substance, in duplicate, in both the presence and absence of S9. Unless limited by solubility, the test substance will be evaluated at a maximum concentration of 5000 µg/plate. Unless indicated otherwise by the Sponsor, the dose levels will be 5000, 1500, 500, 150, 50.0, 15.0, 5.00 and 1.50 µg/plate. If limited by solubility in the vehicle, the test substance will be evaluated at the highest concentration permissible as a workable suspension. Dose levels for the confirmatory mutagenicity assay will be based upon post-treatment toxicity, the precipitation profile, solubility of the test substance and will be documented in the raw data and report. If the top dose is less than 5000 µg/plate due to precipitation or solubility issues, the Sponsor will be consulted. If a retest of the initial toxicity-mutation assay is needed, a minimum of five dose levels of test substance will be used in the retest.

Confirmatory Mutagenicity Assay

TA98, TA100, TA1535, TA1537 and WP2 *uvr*A will be exposed to vehicle alone and at least five concentrations of test substance, in triplicate, in both the presence and absence of S9.

Treatment of Test System

Unless specified otherwise, test substance dilutions will be prepared immediately prior to use. All test substance dosing will be at room temperature under filtered light. One half milliliter (0.5 mL) of S9 mix or Sham mix, 100 µL of tester strain and 50.0 µL of vehicle, test substance dilution or positive control will be added to 2.0 mL of molten selective top agar at 45±2°C. When necessary, aliquots of other than 50.0 µL of test substance or vehicle or positive control will be plated. When plating untreated controls, the addition of test substance, vehicle and positive control will be omitted. The mixture will be vortex mixed and overlaid onto the surface of a minimal bottom agar plate. After the overlay has solidified, the plates will be inverted and incubated for 48 to 72 hours at 37±2°C. Plates that are not counted immediately following the incubation period will be stored at 2-8°C.

Scoring

The condition of the bacterial background lawn will be evaluated for evidence of test substance toxicity and precipitate. Evidence of toxicity will be scored relative to the vehicle control plate and recorded along with the revertant count for that plate. Toxicity will be evaluated as a decrease in the number of revertant colonies per plate and/or a thinning or disappearance of the bacterial background lawn. Precipitation will be evaluated after the incubation period by visual examination without magnification. As appropriate, colonies will be enumerated either by hand or by machine.

Tester Strain Verification
On the day of use in the initial toxicity-mutation assay and the confirmatory mutagenicity assays, all tester strain cultures will be checked for the appropriate genetic markers.

9. CRITERIA FOR DETERMINATION OF A VALID TEST

The following criteria must be met for the initial toxicity-mutation assay and the confirmatory mutagenicity assay to be considered valid. If one or more of these parameters are not acceptable, the affected condition(s) will be retested.

Tester Strain Integrity
To demonstrate the presence of the *rfa* mutation, all *S. typhimurium* tester strain cultures must exhibit sensitivity to crystal violet. To demonstrate the presence of the *uvr*B mutation, all *S. typhimurium* tester strain cultures must exhibit sensitivity to ultraviolet light. To demonstrate the presence of the *uvr*A mutation, all *E. coli* tester strain cultures must exhibit sensitivity to ultraviolet light. To demonstrate the presence of the pKM101 plasmid R-factor, tester strain cultures of TA98 and TA100 must exhibit resistance to ampicillin.

Vehicle Controls Values
Based on historical control data (95% control limits), all tester strain cultures must exhibit characteristic numbers of spontaneous revertants per plate with the vehicle controls. The mean revertants per plate must be within the following ranges (inclusive). Untreated controls, when part of the design, must also be within the ranges cited below.

95% Control Limits (99% Upper Limit)					
	TA98	TA100	TA1535	TA1537	WP2 *uvr*A
-S9	5-25 (30)	66-114 (126)	4-20 (24)	2-14 (17)	10-38 (45)
+S9	10-34 (40)	66-122 (136)	4-20 (24)	3-15 (18)	13-41 (48)
With Study Director justification, values including the 99% control limit and above are acceptable.					

Tester Strain Titers
To ensure that appropriate numbers of bacteria are plated, all tester strain culture titers must be equal to or greater than 0.3×10^9 cells per milliliter.

Positive Control Values
Each mean positive control value must exhibit at least a 3.0-fold increase over the respective mean vehicle control value for each tester strain and exceed the corresponding acceptable vehicle control range cited above.

Toxicity
A minimum of three non-toxic dose levels will be required to evaluate assay data. A dose level is considered toxic if it causes a >50% reduction in the mean number of

revertants per plate relative to the mean vehicle control value (this reduction must be accompanied by an abrupt dose-dependent drop in the revertant count) or a reduction in the background lawn. In the event that less than three non-toxic dose levels are achieved, the affected portion of the assay will be repeated with an appropriate change in dose levels.

10. EVALUATION OF TEST RESULTS

For the test substance to be evaluated positive, it must cause a dose-related increase in the mean revertants per plate of at least one tester strain over a minimum of two increasing concentrations of test substance as specified below:

Strains TA1535 and TA1537

Data sets will be judged positive if the increase in mean revertants at the peak of the dose response is equal to or greater than 3.0-times the mean vehicle control value and above the corresponding acceptable vehicle control range.

Strains TA98, TA100 and WP2 *uvr*A

Data sets will be judged positive if the increase in mean revertants at the peak of the dose response is equal to or greater than 2.0-times the mean vehicle control value and above the corresponding acceptable vehicle control range.

An equivocal response is an increase in a revertant count that is greater than the acceptable vehicle control range but lacks a dose response or does not achieve the respective fold increase threshold cited. A response will be evaluated as negative, if it is neither positive nor equivocal.

11. ELECTRONIC DATA COLLECTION SYSTEMS

Electronic systems used for the collection or analysis of data may include but not be limited to the following (version numbers are maintained in the system documentation):

System	Purpose
LIMS Labware System	Test Substance Tracking
Excel (Microsoft Corporation)	Calculations
Sorcerer Colony Counter and Ames Study Manager (Perceptive Instruments)	Data Collection/Table Creation
Kaye Lab Watch Monitoring system (Kaye GE)	Environmental Monitoring
BRIQS	Deviation and audit reporting

12. REPORT

A report of the results of this study will accurately describe all methods used for generation and analysis of the data. The report will include, but not limited to information about the following:

- Test substance
- Vehicle
- Strains

- Test conditions
- Results
- Discussion of results
- Conclusion
- Historical Control Data (vehicle and positive controls with ranges, means and standard deviations)
- Copy of the protocol and any amendment
- Contributing reports (if applicable)
- Information about the analyses that characterized the test substance, its stability and the stability and strength of the dosing preparations, if provided by the Sponsor
- Statement of Compliance
- Quality Assurance Statement
- CTD Tables (unless otherwise requested)

The report will be issued as a QA-audited draft. After receipt of the Sponsor's comments a final report will be issued. A GLP Compliance Statement signed by the Study Director will also be included in the final report and will note any exceptions if the characterization of the test substance and/or the characterization of the dose formulations are not performed or provided. Four months after issuance of the draft report, if no communication regarding the study is received from the Sponsor or designated representative, the draft report may be issued as a final report. If all supporting documents have not been provided, the report will be written based on those that are provided.

13. RECORDS AND ARCHIVES

All raw data, the original signed protocol, amendment(s) (if applicable), and the original signed final report will be archived by BioReliance as directed by the applicable SOP. A copy of the draft report, including Study Director and Sponsor comments, if applicable, will be archived electronically by BioReliance. Following the SOP retention period, the Sponsor will be contacted by BioReliance for disposition instructions or return of materials. Slides and/or specimens (as applicable) will be archived at EPL Archives and indexed as such in the BioReliance archive database.

BioReliance reserves the right to retain true copies (i.e. photocopies, scans, microfilm, or other accurate reproductions of the original records) for at least the minimum retention period specified by the relevant regulations.

14. REFERENCES

Ames, B.N., McCann, J. and Yamasaki, E. (1975). Methods for detecting carcinogens and mutagens with the *Salmonella*/mammalian-microsome mutagenicity test. Mutation Research 31:347-364.

Green, M.H.L., and Muriel, W.J. (1976). Mutagen testing using trp^{+} reversion in *Escherichia coli*. Mutation Research 38:3-32.

ISO/IEC 17025:2005, General requirements for the competence of testing and calibration laboratories.

Maron, D.M. and Ames, B.N. (1983). Revised Methods for the *Salmonella* Mutagenicity Test. Mutation Research 113:173-215.

McCann, J. and Ames, B.N. (1976). Detection of carcinogens as mutagens in the *Salmonella*/microsome test: assay of 300 chemicals: discussion. Proc. Natl. Acad. Sci. USA 73:950-954.

McCann, J., Choi, E., Yamasaki, E. and Ames, B.N. (1975). Detection of carcinogens as mutagens in the *Salmonella*/microsome test: assay of 300 chemicals. Proc. Natl. Acad. Sci. USA 72:5135-5139.

OECD Guideline 471 (Genetic Toxicology: Bacterial Reverse Mutation Test). Ninth Addendum to the OECD Guidelines for the Testing of Chemicals, adopted July 21, 1997.

APPROVALS

Sponsor Approval

Study Director and Test Facility Management Approvals

BioReliance Study Director — Date: 01 JUN 2018

BioReliance Study Management — Date: 01-Jun-18

15. APPENDIX III: Common Technical Document Tables

2.6.7.8 Genotoxicity: In Vitro

Report Title: Bacterial Reverse Mutation Assay

Test for Induction of: Reverse mutation in bacterial cells

Species/Strain: *S. typhimurium* TA98, TA100, TA1535, TA1537; *E. coli* WP2 *uvr*A

Metabolizing System: Aroclor-induced rat liver S9

Vehicle for Test Substance: Water

Treatment: Plate incorporation

Cytotoxic Effects: None

Genotoxic Effects: None

No. of Independent Assays: 2

No. of Replicate Cultures: 2 (B1) and 3 (B2)

Test Substance:

Study No.: AF28PN.503.BTL

No. Cells Analyzed/Culture: 0.8 to 2.9 x 10^8 cells per plate

GLP Compliance: Yes

Vehicle for Positive Controls: DMSO, except sterile water for sodium azide

Date(s) of Treatment: 05 June 2018 (B1) and 19 June 2018 (B2)

Metabolic Activation	Test Substance	Dose Level (µg/plate)	Revertant Colony Counts (Mean ±SD) (B1: Initial Toxicity-Mutation Assay)				
			TA98	TA100	TA1535	TA1537	WP2uvrA
Without Activation	Water	100 µL/plate	14 ± 4	79 ± 11	13 ± 2	6 ± 4	34 ± 1
		1.50	10 ± 1	80 ± 21	11 ± 8	7 ± 1	36 ± 15
		5.00	9 ± 0	85 ± 2	7 ± 0	7 ± 0	35 ± 13
		15.0	12 ± 3	75 ± 11	12 ± 1	7 ± 1	38 ± 12
		50.0	14 ± 6	88 ± 11	13 ± 2	6 ± 1	30 ± 4
		150	11 ± 5	88 ± 1	9 ± 1	5 ± 2	34 ± 7
		500	14 ± 1	79 ± 4	13 ± 0	7 ± 0	31 ± 5
		1500	19 ± 6	78 ± 3	10 ± 0	5 ± 3	36 ± 6
		5000	11 ± 4	90 ± 8	10 ± 6	6 ± 0	35 ± 0
	2NF	1.00	69 ± 21				
	SA	1.00		600 ± 35	564 ± 21		
	9AAD	75.0				858 ± 120	
	MMS	1000					513 ± 25
With Activation	Water	100 µL/plate	21 ± 8	101 ± 7	14 ± 5	6 ± 1	30 ± 4
		1.50	18 ± 2	98 ± 4	7 ± 1	5 ± 2	33 ± 11
		5.00	17 ± 8	102 ± 6	11 ± 4	6 ± 1	31 ± 1
		15.0	22 ± 5	101 ± 4	12 ± 4	4 ± 1	29 ± 6
		50.0	17 ± 0	106 ± 1	13 ± 4	4 ± 2	29 ± 4
		150	16 ± 3	125 ± 23	13 ± 6	7 ± 2	30 ± 1
		500	23 ± 1	98 ± 1	12 ± 3	4 ± 3	32 ± 1
		1500	29 ± 4	104 ± 15	12 ± 2	8 ± 1	37 ± 8
		5000	16 ± 1	108 ± 7	18 ± 6	5 ± 2	35 ± 1
	2AA	1.00	239 ± 19		83 ± 6		
	2AA	2.00		547 ± 7		70 ± 26	
	2AA	15.0					247 ± 16

Key to Positive Controls

SA	sodium azide	2NF	2-nitrofluorene
2AA	2-aminoanthracene	MMS	methyl methanesulfonate
9AAD	9-Aminoacridine		

Metabolic Activation	Test Substance	Dose Level (µg/plate)	Revertant Colony Counts (Mean ±SD) (B2: Confirmatory Mutagenicity Assay)				
			TA98	TA100	TA1535	TA1537	WP2uvrA
Without Activation	Water	100 µL/plate	13 ± 2	77 ± 9	12 ± 3	5 ± 2	33 ± 3
		50.0	13 ± 4	83 ± 8	10 ± 5	6 ± 3	24 ± 9
		150	13 ± 3	83 ± 3	16 ± 1	7 ± 4	40 ± 9
		500	11 ± 3	92 ± 6	9 ± 2	7 ± 2	34 ± 6
		1500	13 ± 5	89 ± 9	10 ± 4	5 ± 0	37 ± 4
		5000	13 ± 3	73 ± 22	12 ± 4	4 ± 2	35 ± 1
	2NF	1.00	52 ± 14				
	SA	1.00		653 ± 24	590 ± 30		
	9AAD	75.0				521 ± 129	
	MMS	1000					462 ± 38
With Activation	Water	100 µL/plate	14 ± 2	100 ± 7	10 ± 2	6 ± 1	29 ± 5
		50.0	17 ± 5	89 ± 2	8 ± 2	7 ± 2	31 ± 3
		150	17 ± 4	101 ± 4	10 ± 4	5 ± 3	36 ± 9
		500	14 ± 4	94 ± 10	8 ± 2	6 ± 1	34 ± 6
		1500	15 ± 2	92 ± 10	12 ± 1	5 ± 2	31 ± 3
		5000	14 ± 1	94 ± 5	13 ± 5	8 ± 3	31 ± 2
	2AA	1.00	217 ± 15		74 ± 16		
	2AA	2.00		778 ± 19		40 ± 6	
	2AA	15.0					289 ± 1

Key to Positive Controls

SA	sodium azide
2AA	2-aminoanthracene
9AAD	9-Aminoacridine
2NF	2-nitrofluorene
MMS	methyl methanesulfonate

CBI SUBSTANTIATION
PMN/SNUN filing

This Document Contains CBI: Yes☒ NO☐

Technical Contact:

Technical Contact Phone Number: | **Submission number (if known):** Click here.

Submitting Company Name:

Information element(s) claimed as CBI: Please identify the appropriate information element(s) that you are substantiating from the list below. For any information element that is not specifically identified as subject to a confidentiality claim and substantiated as such in your response to this letter, it shall be determined that you have waived your CBI claim, pursuant to 40 C.F.R. § 2.205(d).

You are responsible for substantiating each information element claimed as CBI. If a single substantiation response applies for all information claimed as CBI, you should indicate this in your substantiation response. If different substantiation responses are necessary to support CBI claims for different information types, you should provide separate substantiation responses for each information type, clearly identifying the information for which each substantiation applies in the free text boxes (e.g. Question B) or in the additional information box at the end of this form.

☐ Type of Notice (Page 1)	☒ Byproducts (Part I Section B.7)
☒ Signature and Date of Authorized Official (Page 2)	☒ Production Volume (Part I Section C.1)*
☐ Signature and Date of Agent (Page 2)	☒ Category of Use (Part I Section C.2.a.1)*
☒ Person Submitting Notice (Part I Section A.1.a)	☒ Use Production (Part I Section C.2.a.4)*
☐ Agent (Part I Section A.1.b)	☒ % in Formulation (Part I Section C.2.a.6)*
☐ Joint Submitter (Part I Section A.1.c)	☒ % of Substance Expected Per Use (Part I Section C.2.a.8)*
☒ Technical Contact (Part I Section A.2)	☐ Generic Use Description (Part I Section C.2.b)
☒ Prenotice Communication (PC) (Part I Section A.3)	☒ Site Identity (Part II Section A.1.a)
☒ Previously Submitted Exemption Application (Part I Section A.4)	☒ Site Operations (Part II Section A.1.b)
☒ Previously Submitted Bona Fide (Part I Section A.5)	☒ Amount and Duration (Part II Section A.1.c)*
☐ Type of Notice (Part I Section A.6)	☒ Process Description (Part II Section A.1.d)*
☒ Chemical Class (Part I Section B.1.a)	☒ Worker Activity (Part II Section A.2.1)
☒ Chemical Name/CAS Registry Number (Part I Section B.1.b)**	☒ Protective Equipment/Engineering Controls (Part II Section A.2.3)
☐ Method (Part I Section B.1.c)	☒ Physical Form(s) & % New Substance (Part II Section A.2.5)
☒ Molecular Formula (Part I Section B.1.d)**	☒ # of Workers Exposed (Part II Section A.2.8)
☒ Chemical Structure Diagram for Class I (Part I Section B.1.e)**	☒ Maximum Duration (Part II Section A.2.10-11)
☐ Precursor Substances Class II (Part I Section B.1.e.1)*	☒ Release Number and Amount of New Substance Released (Part II Section A.3.1-2)
☐ Reaction or Process for Class II (Part I Section B.1.e.2)*	☒ Medium of Release and Control Technology and Efficiency (Part II Section A.3.4-5)
☐ Range of Composition and Typical Composition for Class II (Part I Section B.1.e.3)*	☐ Destinations of Releases to Water (Part II Section A.3.7)
☐ Polymer Information (Part I Section B.2.a)**	☐ Operation Description (Part II Section B.1)*

☐ Monomer or Other Reactant Specific Chemical Name (Part I Section B.2.b.1)*	☐ Letter of Activity and # of Workers Exposed (Part II Section B.2.1-2)
☐ Monomer or Other Reactant Specific Chemical Name Typical Composition (Part I Section B.2.b.3)	☐ Duration of Exposure (Part II Section B.2.4)
☐ Monomer or Other Reactant Specific Chemical Name Include in Identity (Part I Section B.2.b.4)*	☐ Protective Equipment/Engineering Controls/Physical Form/ % New Substance/% in Formulation (Part II Section B.2.6-7)
☐ Monomer or Other Reactant Specific Chemical Name Max Residual (Part I Section B.2.b.6)	☐ Release Number and Amount of New Substance Released (Part II Section B.2.9-10)
☐ Method Used to Obtain Specific Chemical Identity (Part I Section B.2.c)	☐ Media of Release & Control Technology (Part II Section B.2.12)
☐ Current Chemical Abstracts (CA) Name and Number for Polymer (Part I Section B.2.d)**	☐ Byproducts (Part II Section B.2.14)
☐ Chemical Structure Diagram (Part I Section B.2.e)**	☒ Pollution Prevention Information (PMN page 11, form page 16)
☒ Impurities (Part I Section B.3)	☒ Attachments (Part III, PMN page 12, form page 17)
☒ Synonyms (Part I Section B.4)	☒ Physical and Chemical Properties Worksheet (PMN page 13, Form page 18)***
☐ Trade Identification (Part I Section B.5)	

☒**Other information elements claimed as CBI** (Please list any other CBI claim or any TSCA Section 14(c)(2) assertion not listed above. In some cases, it may be appropriate to group the information into a class of information rather than responding to each item claimed as CBI. If you are asserting a category of information, please identify all information elements within that category):

The supporting data in all health and safety studies was NOT claimed as CBI.

The final study report(s) were redacted as follows:
- chemical identity of the test substance
- all forms of the Company name, logo and addresses
- all Company employee names, addresses, phones numbers and email addresses
- all study sponsor names, addresses, phones numbers and email addresses
- all Company report numbers
- all study sponsor report numbers
- analyte information
- impurity information
- tradenames (including product name)

I. REQUIRED FOR ANY IDENTIFIED CBI CLAIM

A. Do you believe that any information element claimed as CBI is exempt from substantiation pursuant to TSCA section 14(c)(2)[1] ?

☑ Yes
☐ No

If you answered yes, you must identify the specific information element(s), provide the specific exemption(s) and answer no further questions. For any information element that is not exempt, please respond to all of the questions below.

If the Agency disagrees with this assertion, you may be asked to provide additional information to support your claim.

☒ Impurities (Part I Section B.3) – TSCA Section 14(c)(2)(A)
☒ Byproducts (Part I Section B.7) - TSCA Section 14(c)(2)(A)
☒ Production Volume (Part I Section C.1)* - exempt from substantiation
☒ Category of Use (Part I Section C.2.a.1)* - exempt from substantiation
☒ Use Production (Part I Section C.2.a.4)* - exempt from substantiation
☒ % in Formulation (Part I Section C.2.a.6)* - exempt from substantiation
☒ % of Substance Expected Per Use (Part I Section C.2.a.8)* - exempt from substantiation
☒ Process Description (Part II Section A.1.d)*- exempt from substantiation
☒ Protective Equipment/Engineering Controls (Part II Section A.2.3)- TSCA Section 14(c)(2)(A)
☒ Pollution Prevention Information (PMN page 11, form page 16) - TSCA Section 14(c)(2)(E)
☒ Physical and Chemical Properties Worksheet (PMN page 13, Form page 18)*** - exempt from substantiation (this chemical substance is not on the inventory and has not been offered for commercial distribution)

B. Will disclosure of any information element claimed as CBI likely result in substantial harm to your business's competitive position?

☑ Yes
☐ No

(If you answered yes, please describe with specificity the substantial harmful effects that would result to your competitive position if the CBI information element is made available to the public.)

If you are claiming multiple information elements, please make sure to provide information for EACH element you identified above. If a single substantiation response applies for all information claimed as CBI, you should indicate this in your substantiation response.

A single substantiation response applies for all information claimed as CBI.

Disclosure of the claimed CBI would result in harmful effects on submitter's competitive position since the submitter has committed, a significant amount of time, resources, and dollars to the research and development of the PMN substance. Disclosure of the claimed CBI would permit a competitor to specifically know and understand the submitter's research efforts with this PMN substance and to forego the necessary time and expense to develop such a substance, thus capitalizing on the submitter's research and development efforts. This knowledge could be used by competitors to introduce new patents and/or competitive products in the areas of interest to our company which would otherwise reduce the value of this product for our business. In addition, it would be a simple matter for competitors, having gained knowledge of CBI composition and structure, to recreate this PMN substance using common synthetic techniques which could compete in this marketspace, with or without patents, and well as to determine manufacturing cost information from such knowledge, thereby limiting potential competitive advantage.

C. To the extent your business has disclosed any information to others (both internally and externally), what precautions has your business taken? Please identify the measures or internal controls your business has taken to protect the information claimed as confidential.

1. Non-disclosure agreement required prior to access. ☑ Yes ☐ No
2. Access is limited to individuals with a need-to-know ☑ Yes ☐ No
3. Information is physically secured (e.g. locked in room or cabinet) or electronically secured (encrypted, password protected, etc.). ☑ Yes ☐ No
4. Other internal control measure(s). *(If yes please explain below.)* ☑ Yes ☐ No
   Electronic copies of documents containing CBI are kept in restricted databases.

D. Does any of the information claimed as confidential appear in any public documents, including (but not limited to) safety data sheet, advertising or promotional material, professional or trade publication, or any other media or publications available to the general public? *(If you answered yes, please explain why the information should be treated as confidential.)*	☐ Yes ☑ No
The information claimed as confidential does not appear in any public documents, including (but not limited to) safety data sheet, advertising or promotional material, professional or trade publication, or any other media or publications available to the general public. Process patents using the PMN substance are publicly available. The patents teach many examples of compositions. Disclosure of the specific chemical identity of the chemical substance would narrow the compositional scope for a competitor and may permit a modified process to be designed that could circumvent the patent and/or patent applications.	
E. Does any of the information you are claiming as CBI contain (a) trade secret(s)[2] ? *(If you answered yes, please explain the reason for your belief and attach copies of those pages containing such information with brackets around the text that you claim to be (a) trade secret(s).)*	☐ Yes ☑ No
The Agency should work with us to identify approaches to protect our trade secrets and innovation investment while meeting the intent of the CBI regulations.	
F. If you assert a claim of confidentiality that is less than 10 years (see TSCA section 14(e)(1)(B)[3]), then please indicate the number of years (between 1-10 years) or specific date of which the claim is withdrawn[4]?	
The claim of confidentiality is requested permanently, or until the submitter makes the information common knowledge. It is understood that any approved claims will expire after 10 years unless they are re-substantiated.	
G. Has the EPA, another federal agency, or court made any confidentiality determination regarding information associated with this substance? *(If you answered yes, please explain the outcome of that determination and provide a copy of the previous confidentiality determination or any other information that will assist in identifying the prior determination.)*	☐ Yes ☑ No
Click or tap here to enter text.	
Additional comments:	
Click or tap here to enter text.	

II. REQUIRED ONLY FOR CHEMICAL IDENTITY CBI CLAIMS	
A. Are you claiming a specific chemical identity as CBI? *(If you answered yes, please respond to questions below.* *If you answered no, please leave all questions below blank)*	☑ Yes ☐ No
B. Is the chemical substance (or mixture) on the confidential portion of TSCA Inventory?	☐ Yes ☑ No
C. Has the chemical substance (or mixture) been offered for commercial distribution? *(If you answered yes, please explain why the information should be treated as confidential.)*	☐ Yes ☑ No

The chemical substance has NOT been offered for commercial distribution.

D. Is the chemical substance known to be in US commerce? ☐ Yes ☑ No

(If you answered yes, please explain why the information should be treated as confidential.)

Not to the best of our knowledge. MSDSs for the chemical substance disclose only its generic name.

E. Would disclosure of the specific chemical name release confidential process information? ☑ Yes ☐ No

(If you answered yes, please explain why the information should be treated as confidential.)

It is anticipated that a competitor could reverse engineer the PMN substance, if CBI is revealed. Disclosure of the PMN substance identity will result in disclosure of the confidential process by which it is made, since a chemist skilled in organic synthesis would understand from the name what substances are used form the final test substance. The chemical identity of a Class 1 substance, along with its impurities and byproducts, provides much information on the technology used to manufacture these substances.

F. In the case of a mixture, would disclosure of the chemical name disclose a portion of the mixture comprised by any of the chemical substances in the mixture? ☐ Yes ☐ No

(If you answered yes, please explain why the information should be treated as confidential.)

Click or tap here to enter text.

Additional comments:

Click or tap here to enter text.

III. SUBSTANTIATION CERTIFICATION

Do you wish to claim this substantiation as CBI? ☑ Yes ☐ No

TSCA section 14(c) requires that persons asserting a CBI claim shall certify to the validity of the claims. By the marking of a yes, you are certifying to the truth of the below statements.

I hereby certify to the best of my knowledge and belief that all information entered on this form is complete and accurate.

I further certify that, pursuant to 15 U.S.C. § 2613(c), for all claims for confidentiality made with this submission, all information submitted to substantiate such claims is true and correct, and that it is true and correct that

(i) My company has taken reasonable measures to protect the confidentiality of the information;
(ii) I have determined that the information is not required to be disclosed or otherwise made available to the public under any other Federal law;
(iii) I have a reasonable basis to conclude that disclosure of the information is likely to cause substantial harm to the competitive position of my company; and

(iv) I have a reasonable basis to believe that the information is not readily discoverable through reverse engineering.

Any knowing and willful misrepresentation is subject to criminal penalty pursuant to 18 U.S.C. § 1001.

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[*] EPA believes this information element to be exempt from substantiation for this activity.

[**] EPA believes this information element to be exempt from substantiation for this activity (only applies prior to the date on which a chemical substance is first offered for commercial distribution).

[***] EPA believes Spectra information elements to be exempt from substantiation for this activity (only applies prior to the date on which a chemical substance is first offered for commercial distribution).

[1] **"TSCA Section 14(c)(2) states:**

Information generally not subject to substantiation requirements

Subject to subsection (f), the following information shall not be subject to substantiation requirements under paragraph (3):

(A) Specific information describing the processes used in manufacture or processing of a chemical substance, mixture, or article.

(B) Marketing and sales information.

(C) Information identifying a supplier or customer.

(D) In the case of a mixture, details of the full composition of the mixture and the respective percentages of constituents.

(E) Specific information regarding the use, function, or application of a chemical substance or mixture in a process, mixture, or article.

(F) Specific production or import volumes of the manufacturer or processor.

(G) Prior to the date on which a chemical substance is first offered for commercial distribution, the specific chemical identity of the chemical substance, including the chemical name, molecular formula, Chemical Abstracts Service number, and other information that would identify the specific chemical substance, if the specific chemical identity was claimed as confidential at the time it was submitted in a notice under section 2604 of this title.

[2] **"Trade secret"** is defined as "a secret, commercially valuable plan, formula, process, or device that is used for the making, preparing, compounding, or processing of trade commodities and that can be said to be the end product of either innovation or substantial effort." Public Citizen Health Research Group v. FDA, 704 F.2d 1280, 1288 (D.C. Cir. 1983).

[3] **"TSCA section 14(e)(1)(B) States"**

(B) in the case of information other than information described in subsection (c)(2)—

(i) for a period of 10 years from the date on which the person asserts the claim with respect to the information submitted to the Administrator; or

(ii) if applicable before the expiration of such 10-year period, until such time as—

(I) the person that asserted the claim notifies the Administrator that the person is withdrawing the claim, in which case the information shall not be protected from disclosure under this section; or

(II) the Administrator becomes aware that the information does not qualify for protection from disclosure under this section, in which case the Administrator shall take any actions required under subsections (f) and (g).

[4] Information with withdrawn CBI claims will be made available to the public without further notice.